
السلام علیک یا اباعبدالله الحسین

Blood Typing and Blood Transfusion in Dog and Cat

History of Blood Transfusions

- The first human blood transfusion was performed in 1492. Pope Innocent VIII was transfused with blood from 3 young boys. All three boys died (and so did the pope)
- The first recorded successful canine blood transfusion was done by Richard Lower in 1665 between a Mastiff and a mixed breed dog
  - A silver tube was connected to the donor's artery and the recipient's vein

Question …

How long do canine & feline RBC's remain in circulation?

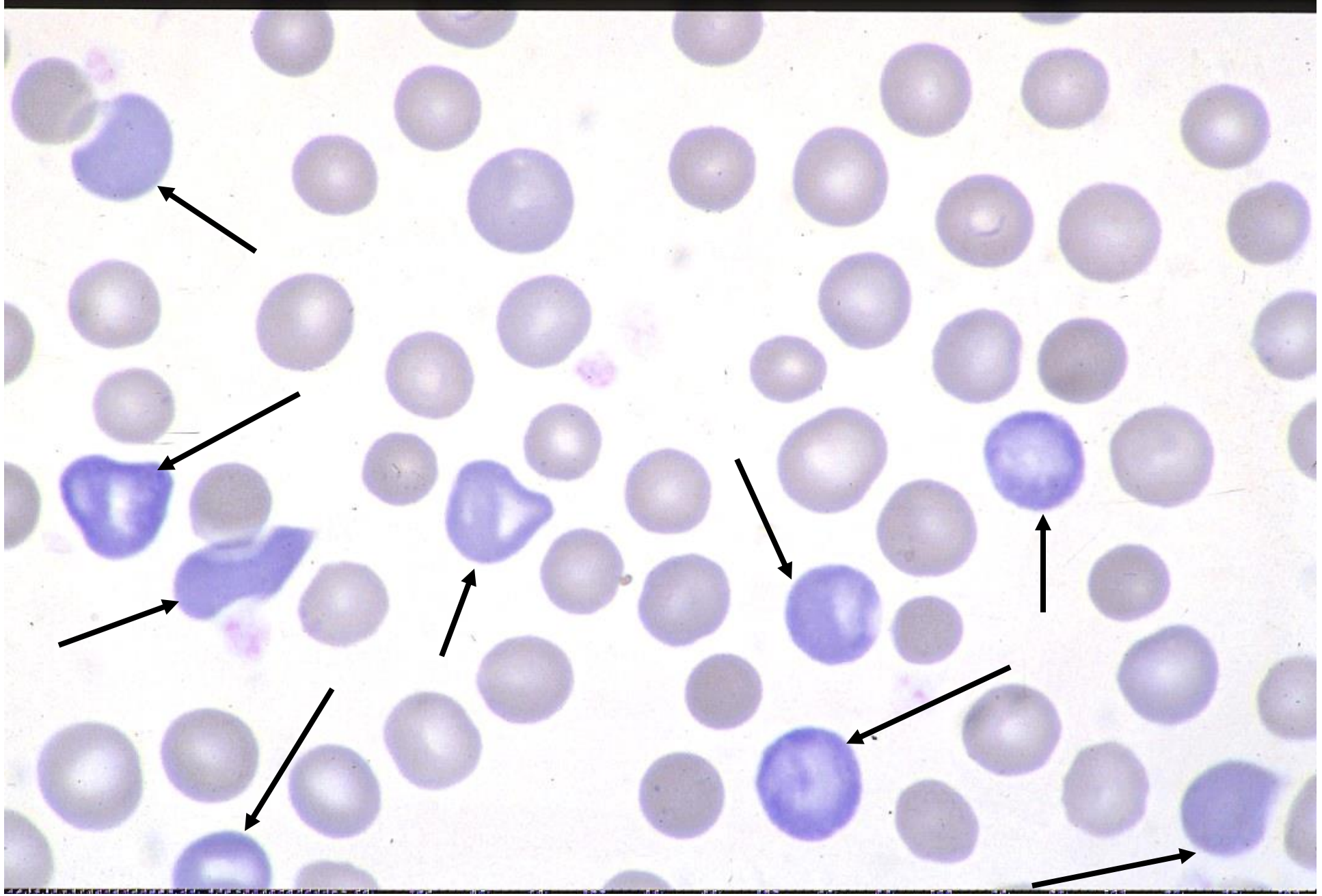
Dog - 110 days

Cat -70 days

Humans – 120 days

Anemia/ Non- Regenerative Anemia

- Anemia- A decrease in red blood cells
  - Bone marrow will respond to this decrease by increasing red blood cell production
- Non-regenerative anemia- the bone marrow response is inadequate when compared to the increased need



Blood Smear

POLYCHROMASIA

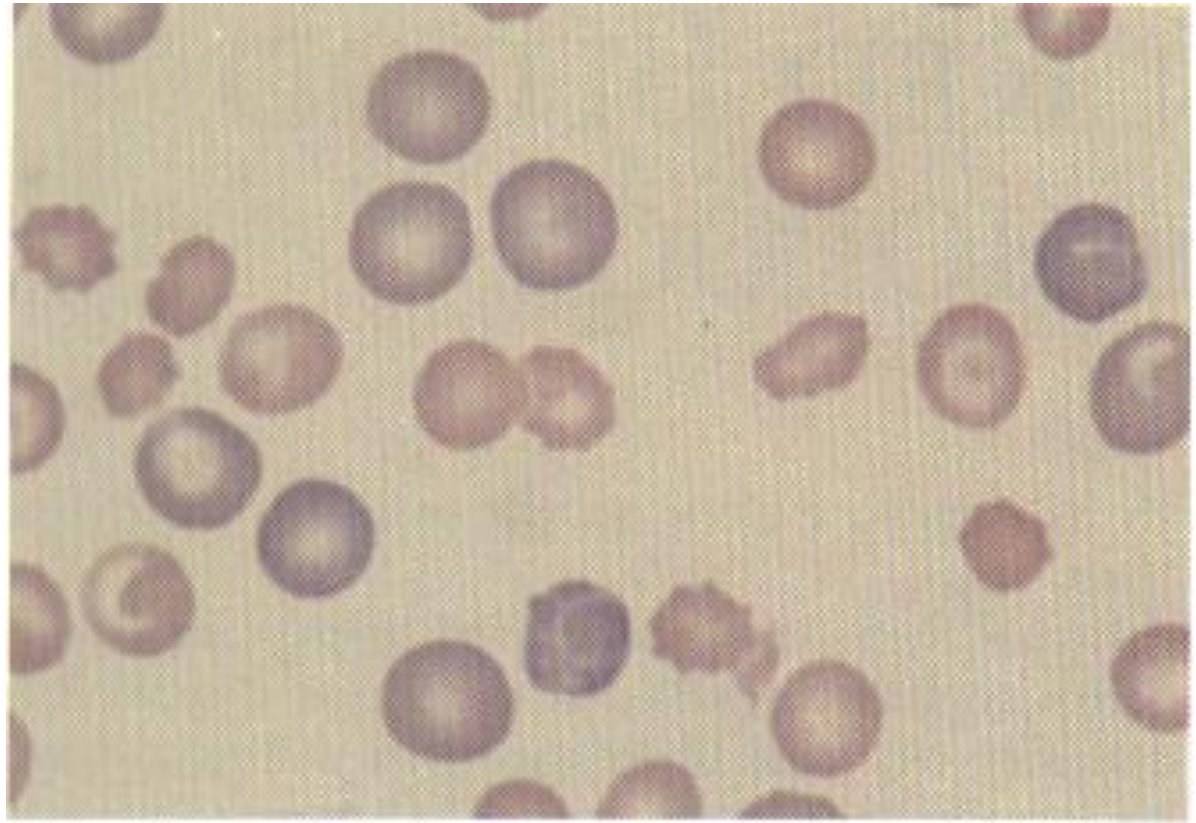


Figure 3.1. Polychromatophils. The bluish-staining, usually larger red blood cells are polychromatophils. In most animals, except horses, polychromatophils are present in high numbers in circulation during a regenerative anemia. In addition, there is slight poikilocytosis and target cells are present. Canine blood smear; 100× objective.

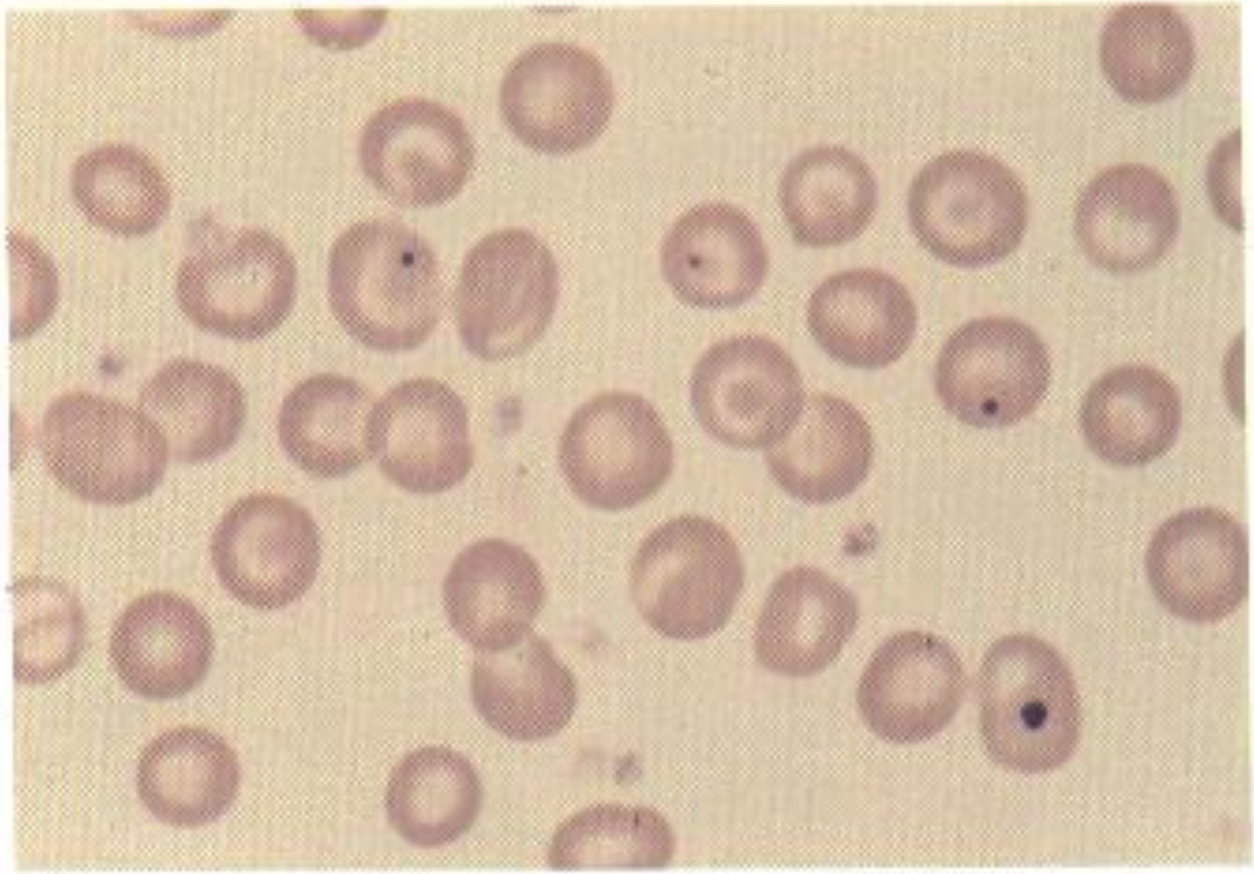
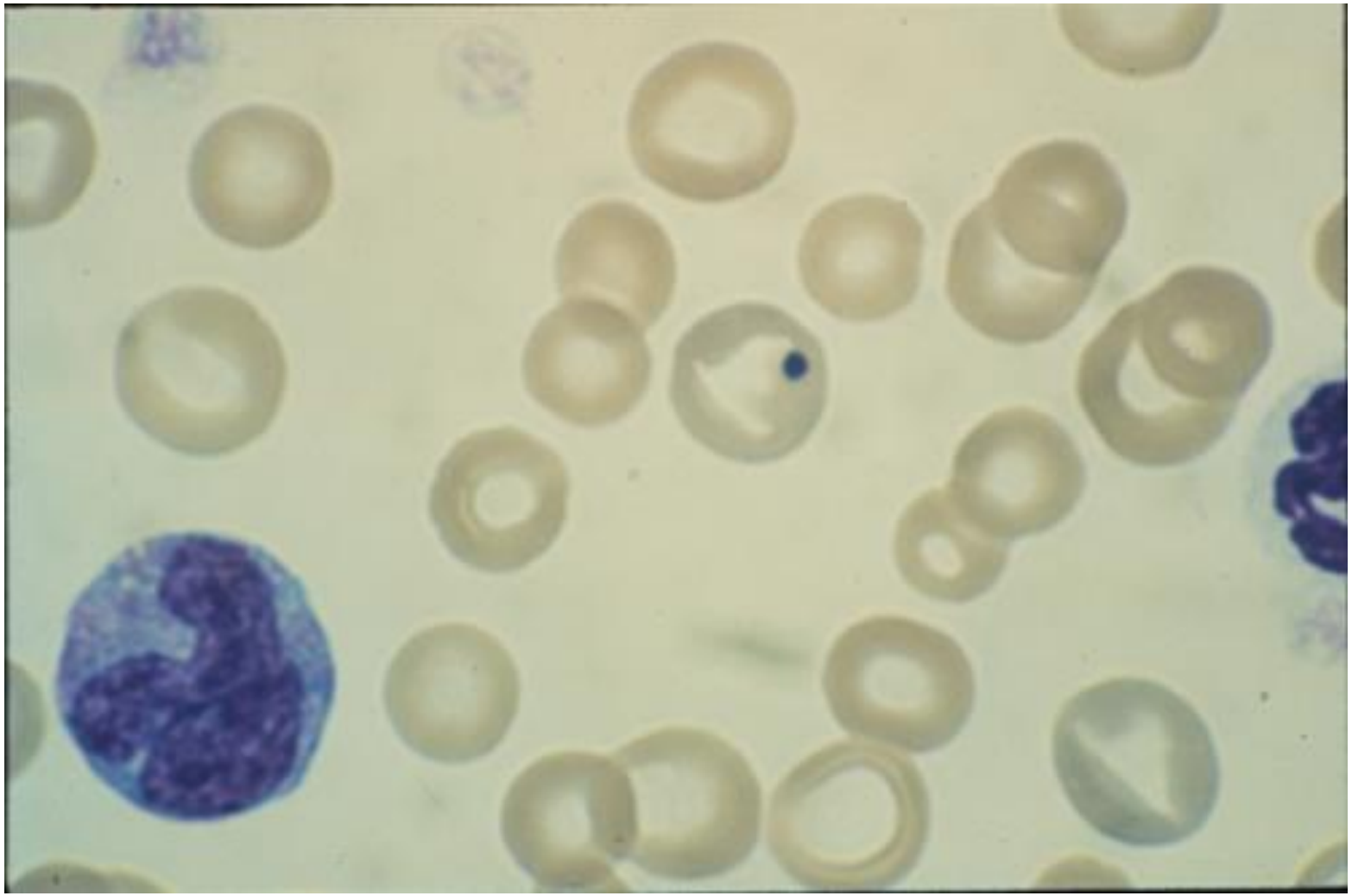


Figure 4.6. Howell-Jolly bodies. Four red blood cells have single, small, round, deep purple cytoplasmic inclusions; these are Howell-Jolly bodies, which are nuclear fragments. Target cells are also present. Canine blood smear; 100× objective.



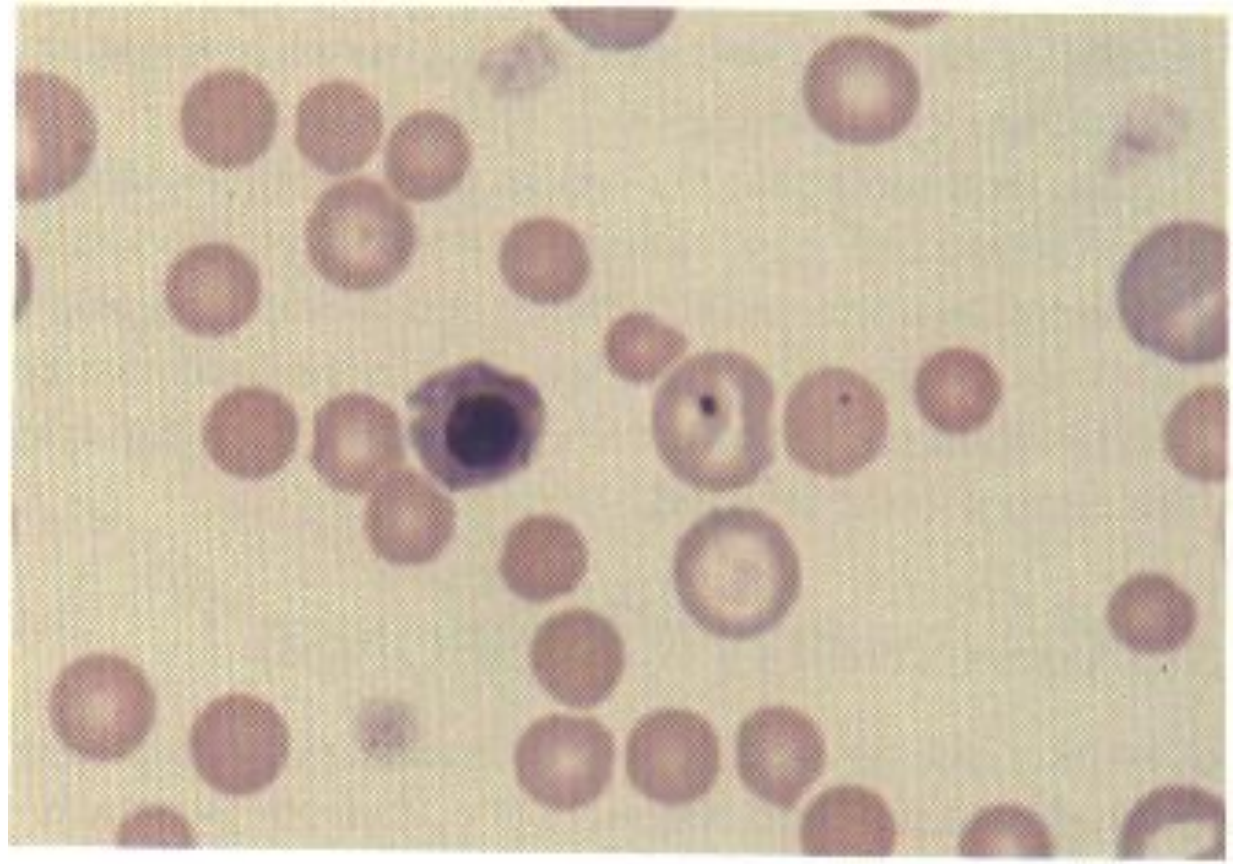
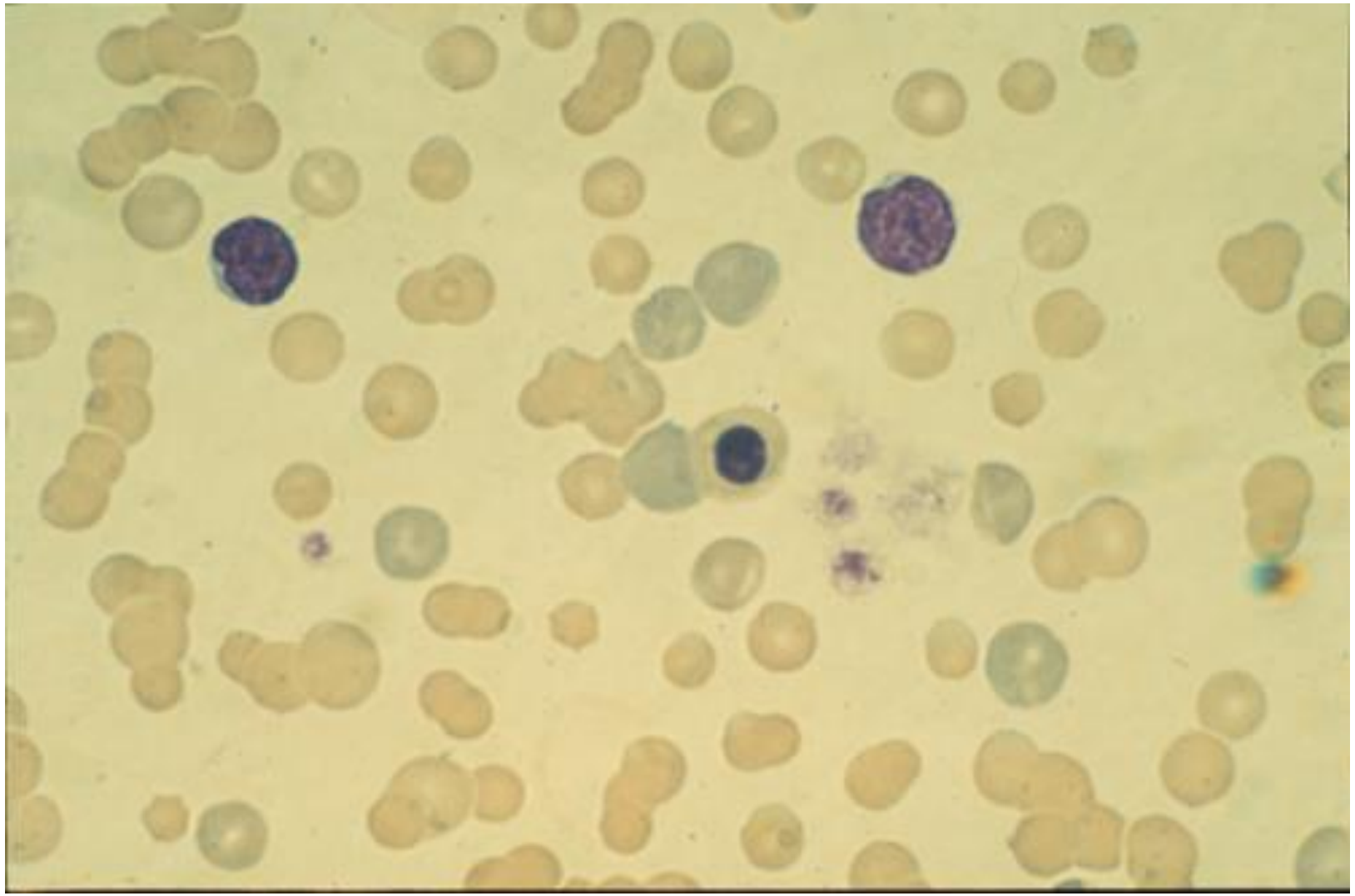


Figure 3.4. Nucleated red blood cell and Howell-Jolly bodies. The slightly blue cell with the round nucleus and condensed chromatin is a nucleated red blood cell (metarubricyte). Two adjacent red blood cells have single, small, round, deep purple cytoplasmic inclusions; these are Howell-Jolly bodies, which are fragments of nuclei. Canine blood smear; 100× objective.



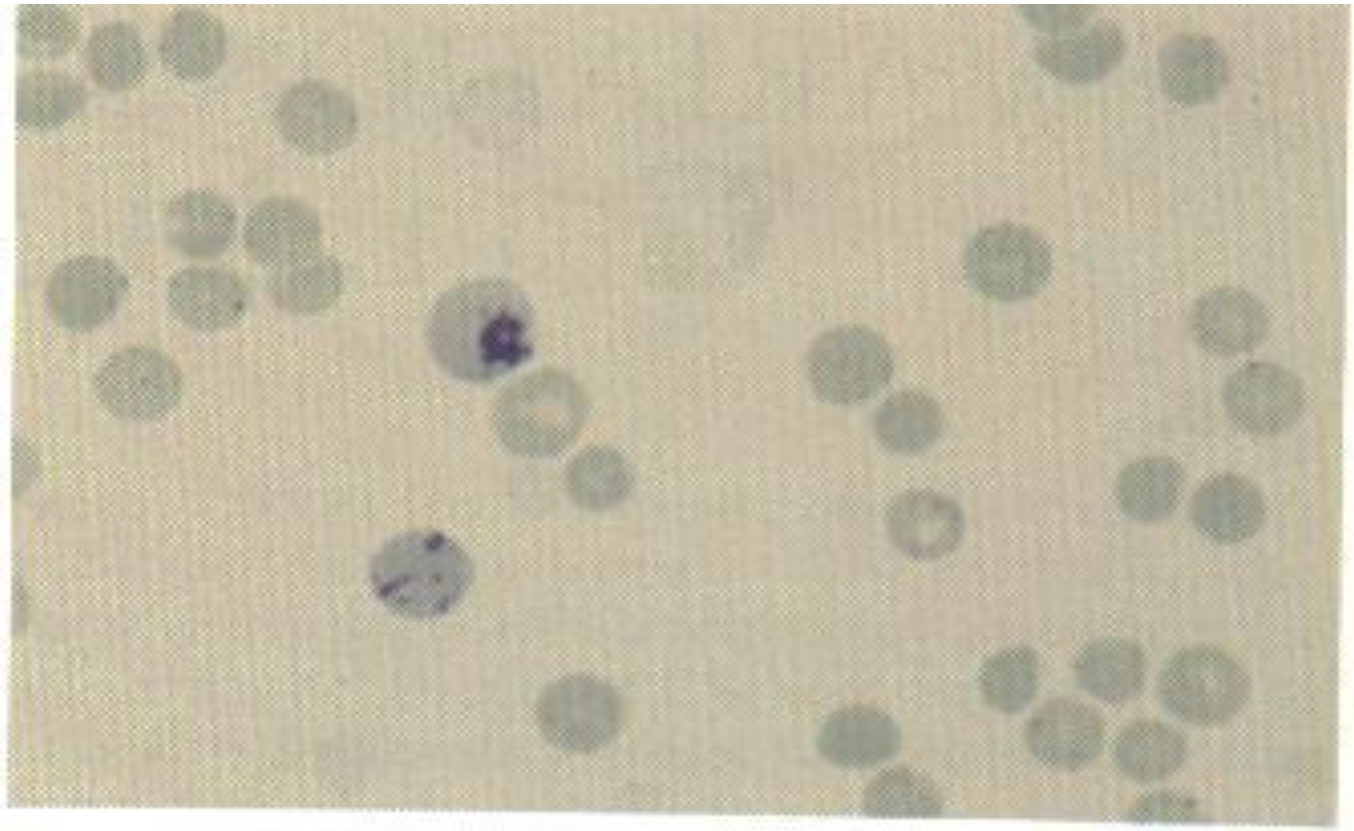


Figure 3.3. Aggregate and punctate reticulocytes. The two cells (left center) that have dark blue, clumped granular material in the cytoplasm are aggregate reticulocytes. The cells with small single or multiple dots of bluish material are punctate reticulocytes. The cells with no reticulum are mature red blood cells. Feline blood smear; new methylene blue stain; 100× objective.

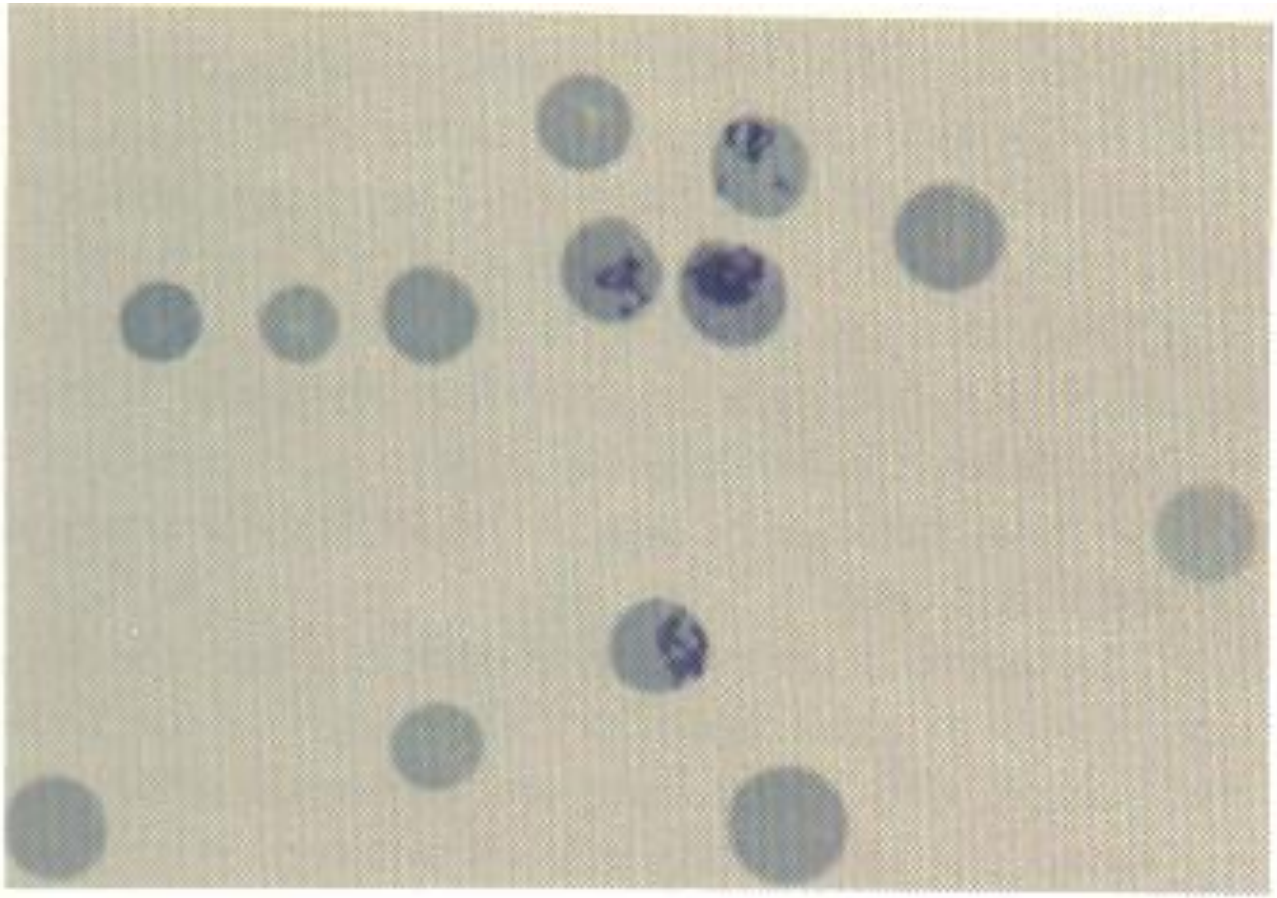
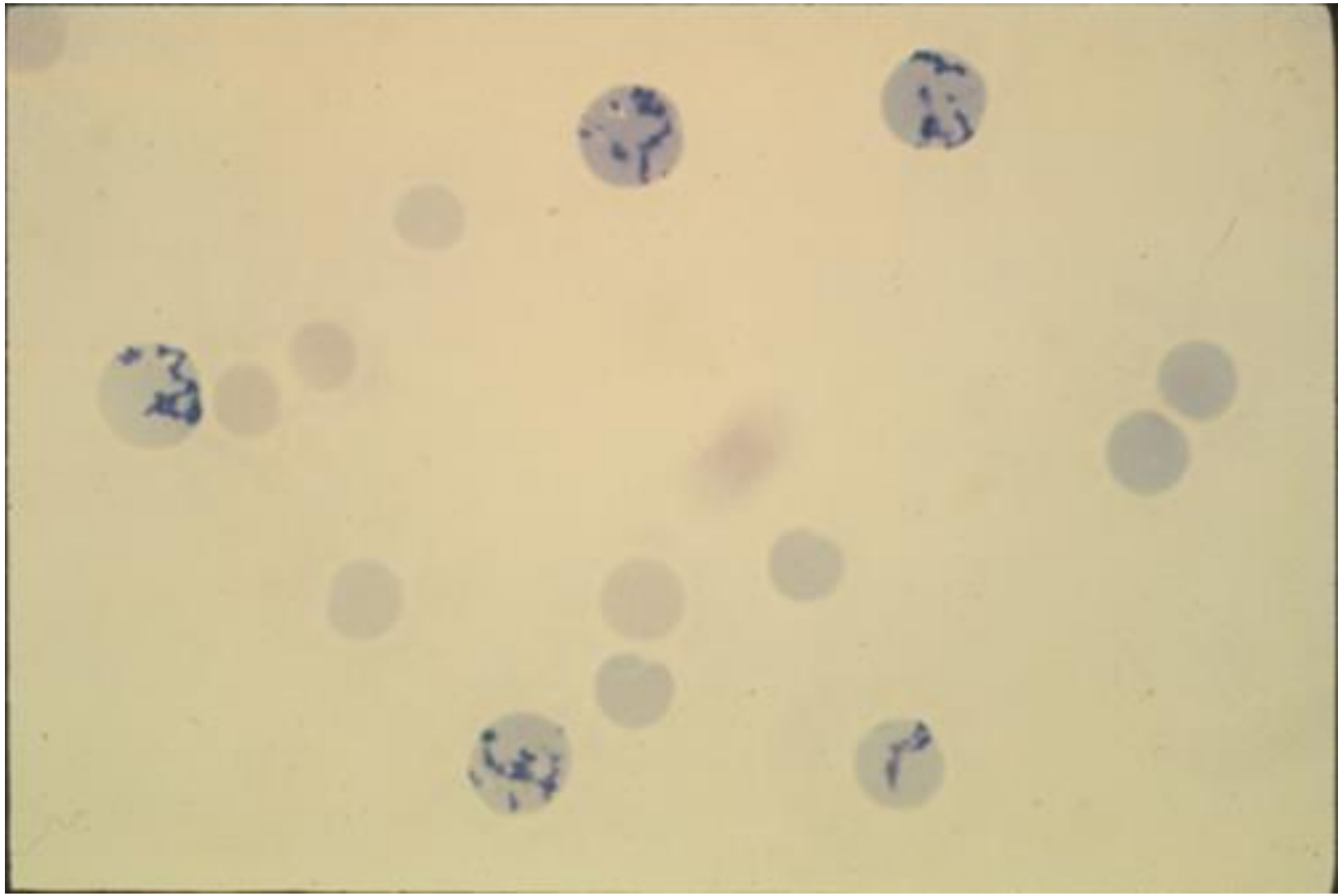


Figure 3.2. Reticulocytes. The four cells with dark blue, clumped granular material (reticulum) in the cytoplasm are reticulocytes. The cells with no reticulum are mature red blood cells. Canine blood smear; new methylene blue stain; 100× objective.



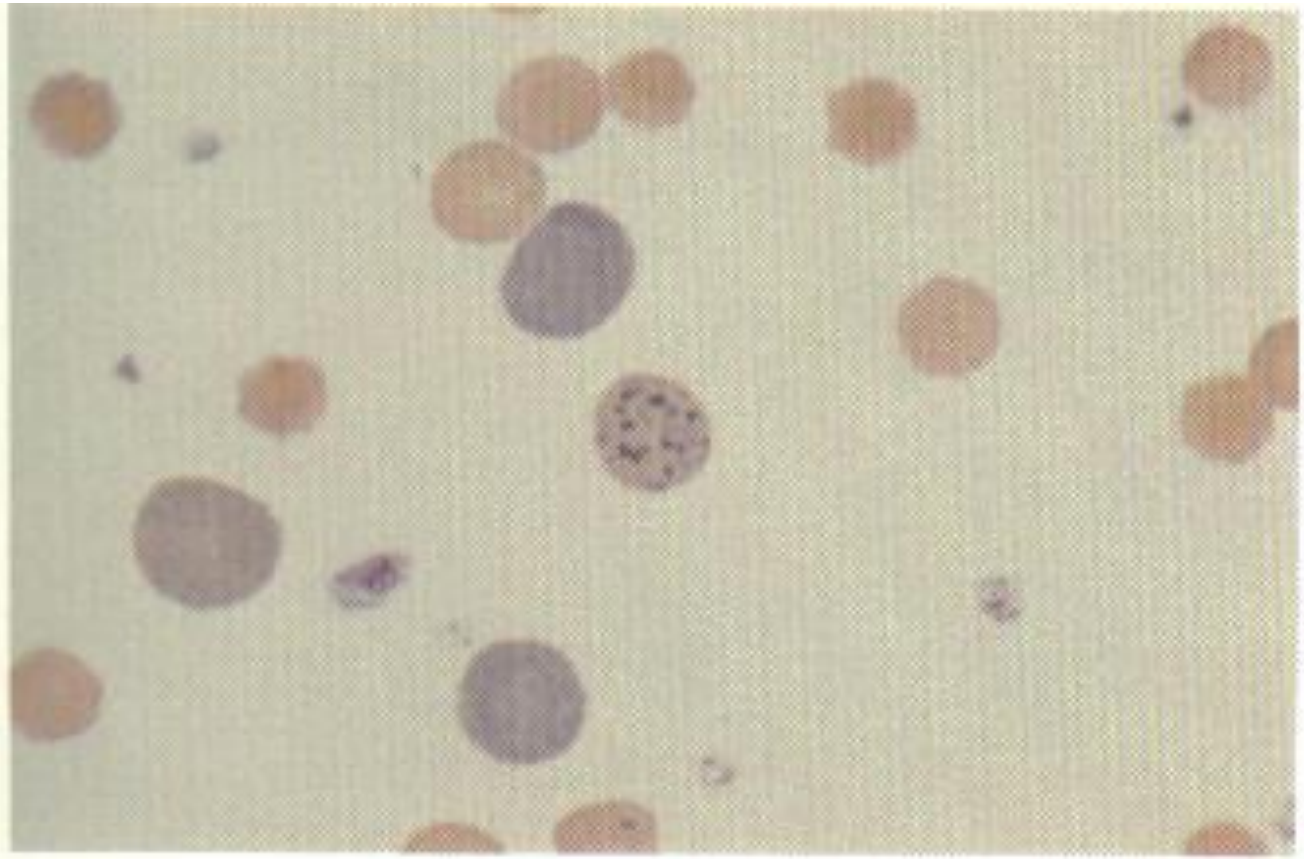
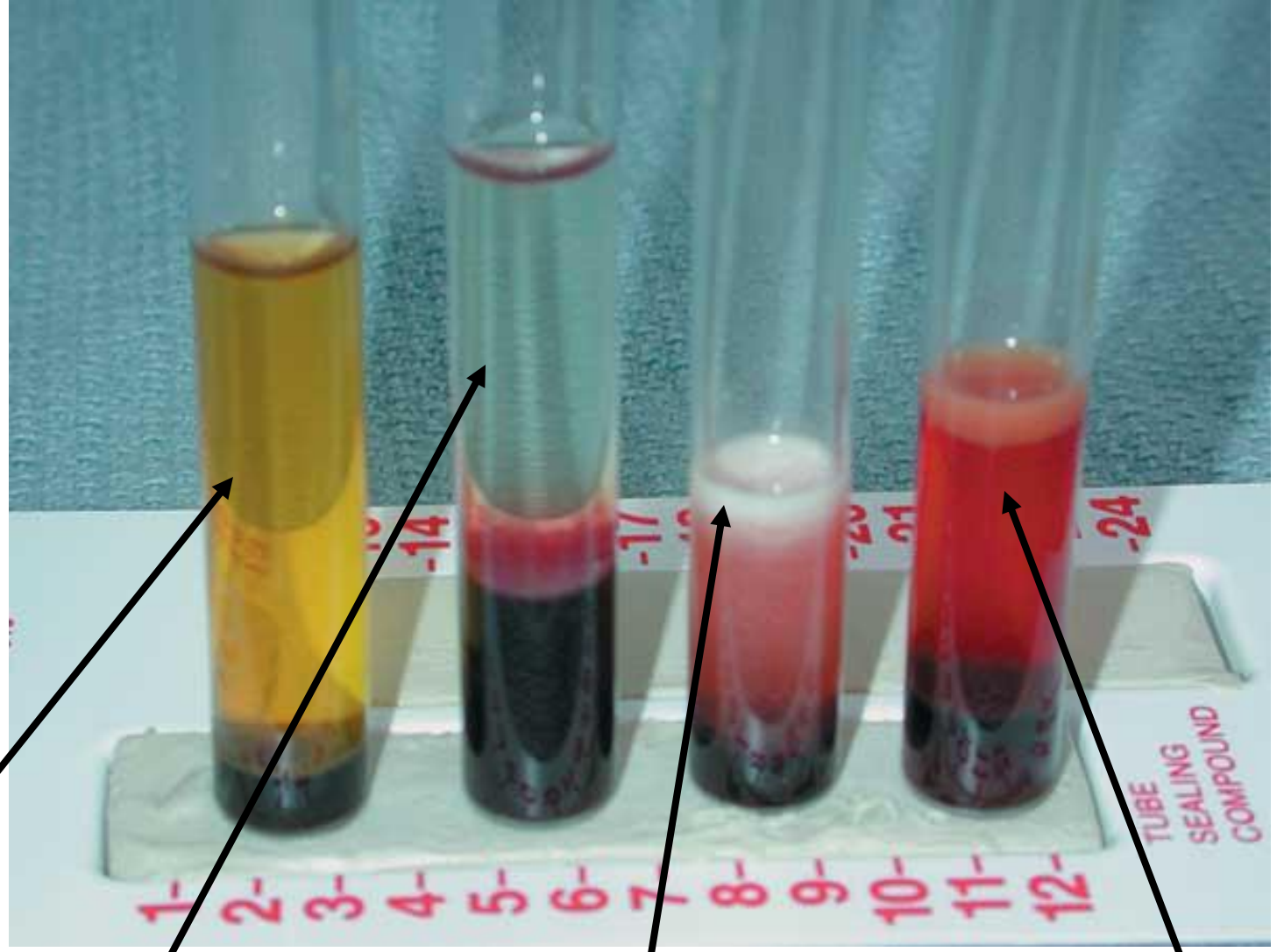
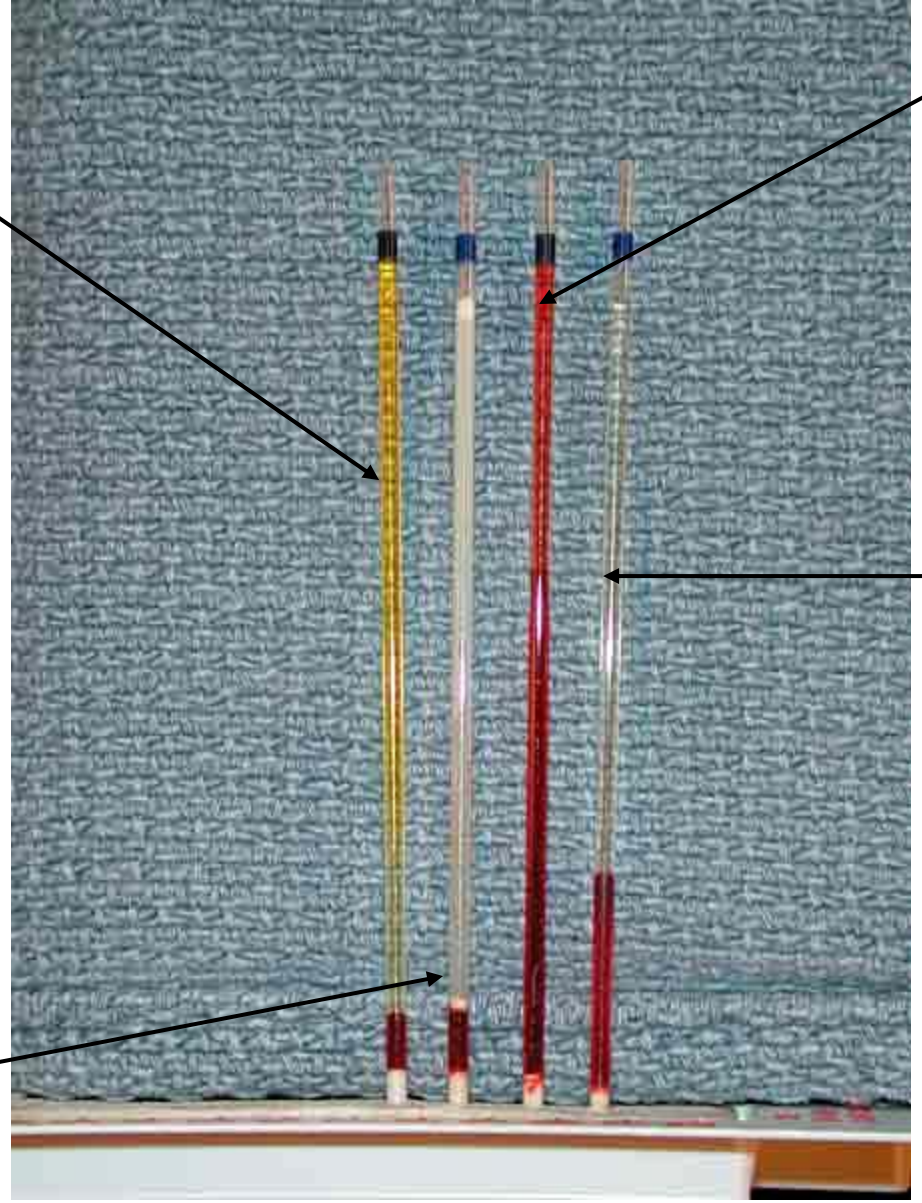


Figure 3.5. Basophilic stippling. The red blood cell (center) with multiple, small blue dots is a red blood cell with basophilic stippling. The three large, bluish-staining red blood cells are polychromatophils. There is moderate anisocytosis present also. Bovine blood smear; 100× objective.


Icteric
Normal
Lipemia w/
hemolysis
Hemolysis
TUBE
SEALING
COMPOUND


Iceteric and anemic
Hemolysis
Normal
Lipemic and anemic

Indications for Blood Transfusions

- **Severe blood loss** (trauma, acute hemorrhage during surgery)
- **Chronic anemia** with respiratory distress and weakness
- **Coagulation defects** (Hemophilia, VonWillebrand disease)
  - Sometimes better to use platelet rich plasma than whole blood
- **Autoimmune Hemolytic Anemia** (AIHA)

Indications in animals

- When HCT has fallen rapidly to below 20% in dogs and 15% in cats.
- Deficiency of blood constituents.
- Autoimmune hemolytic anemia.
- Surgery.
- Babesiosis.
- Theleriosis.
- Anaplasmosis.
- Blood poisoning.
- Abomasal ulcer.
- Pulmonary Hemorrhages.

A general rule is that if an effective alternative is available, transfusion should be avoided.

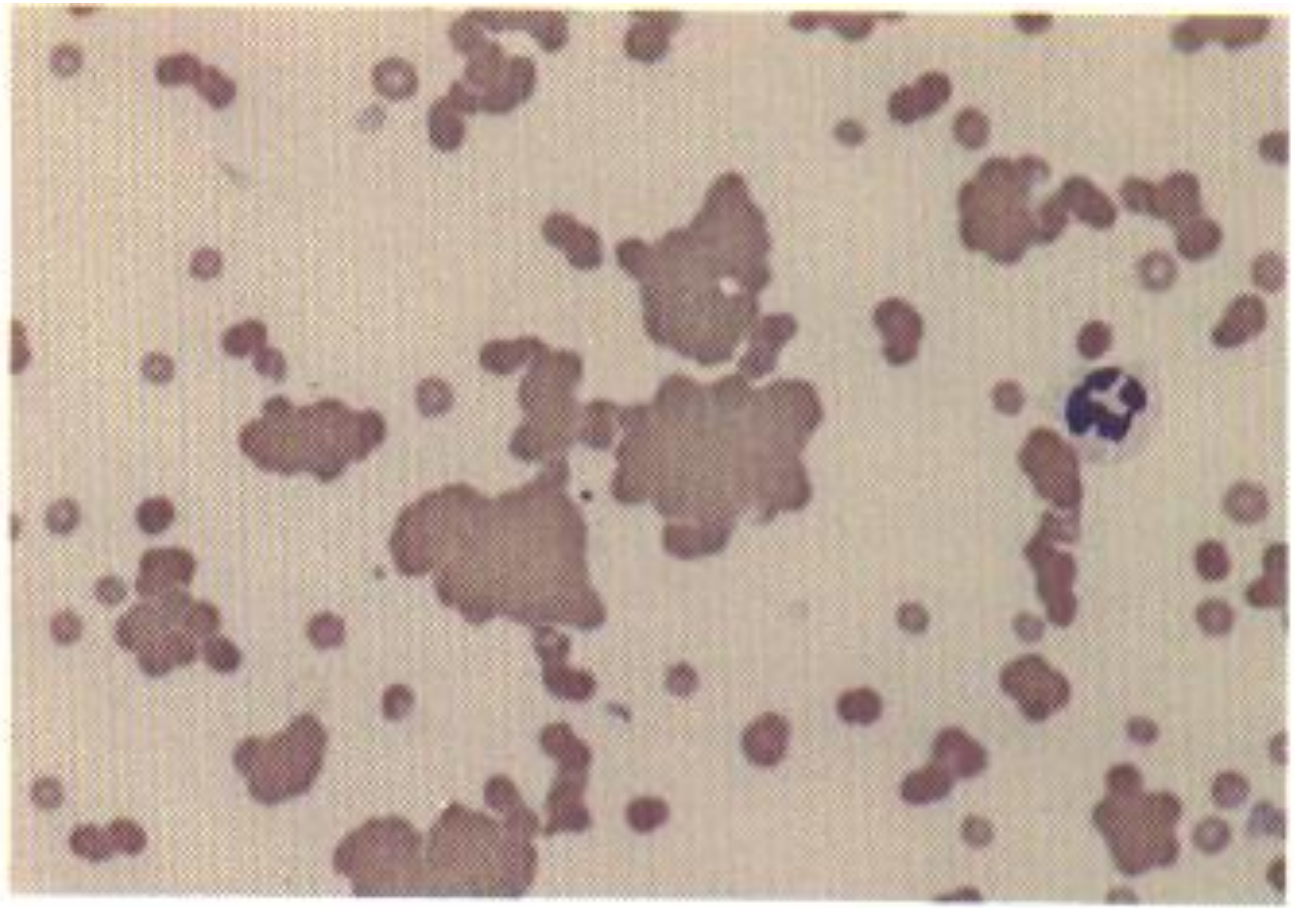
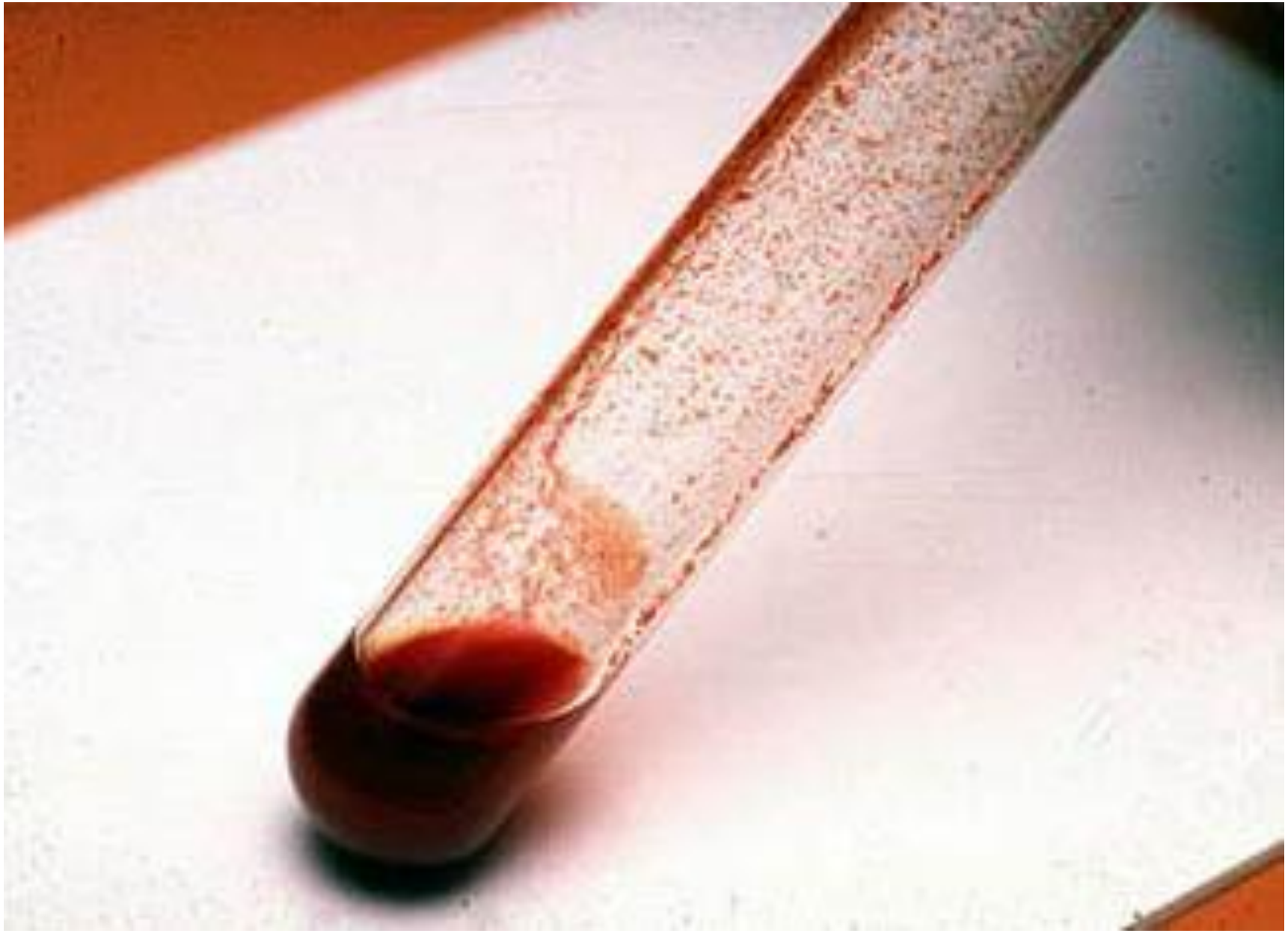
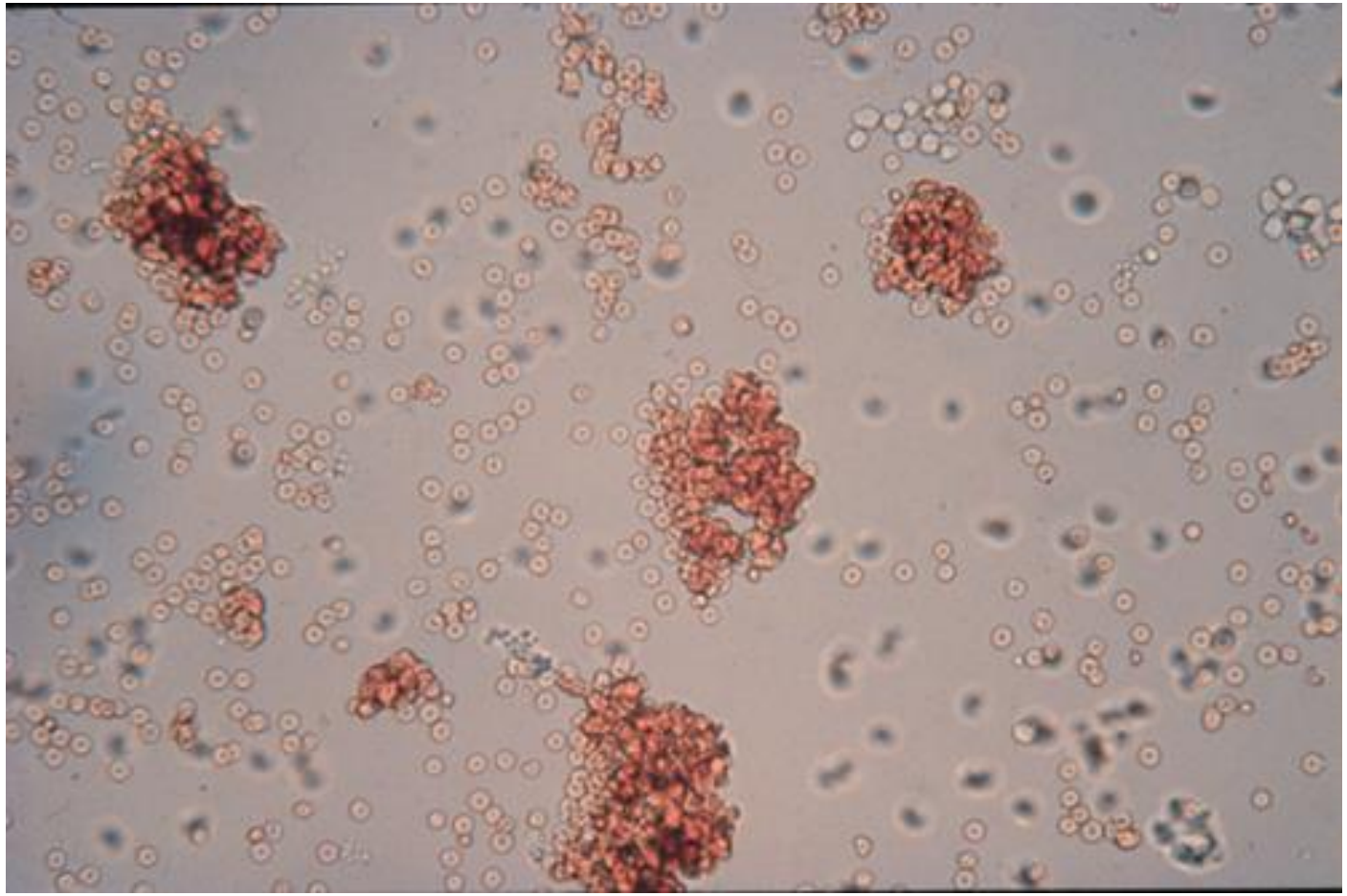
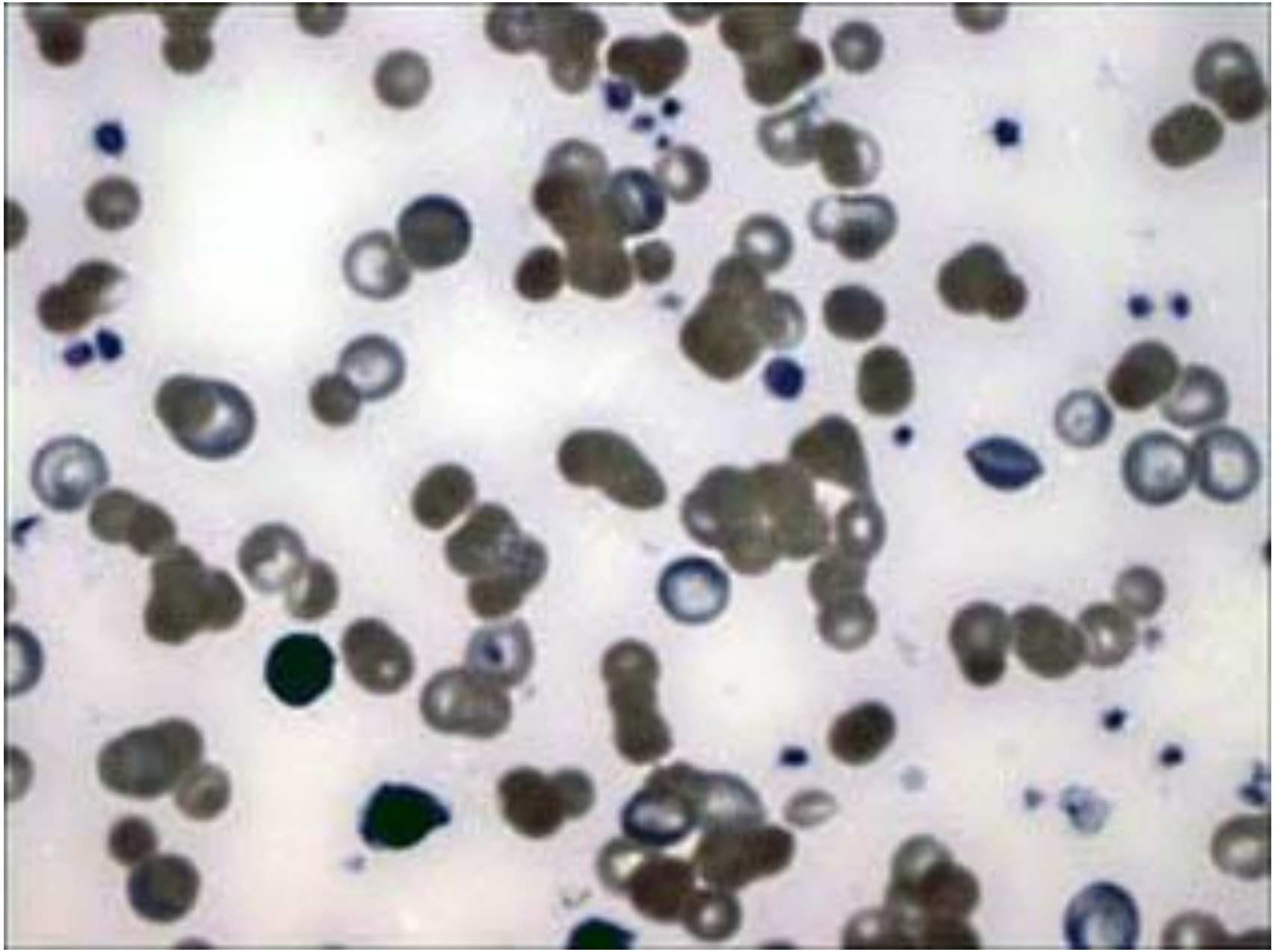
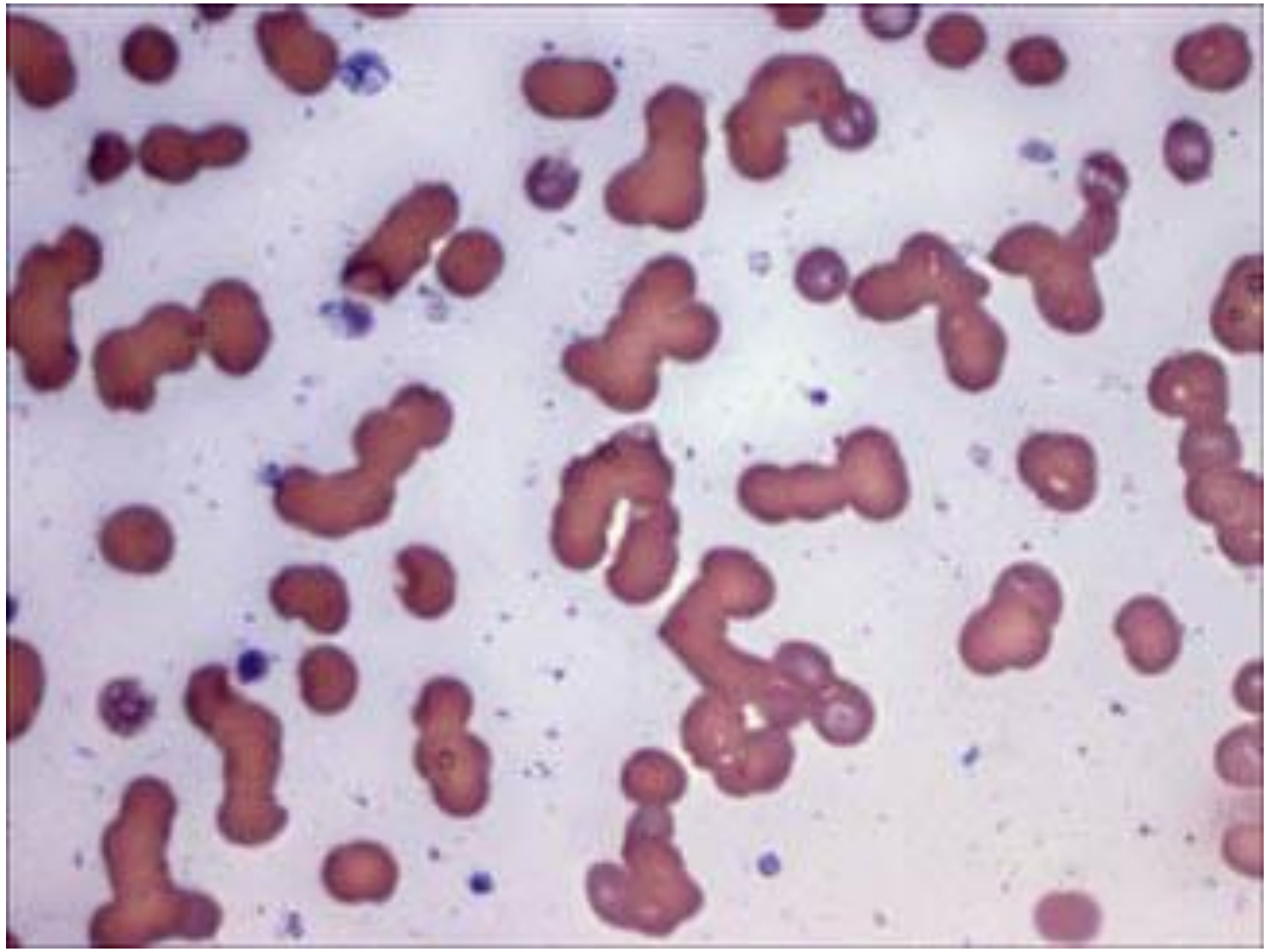


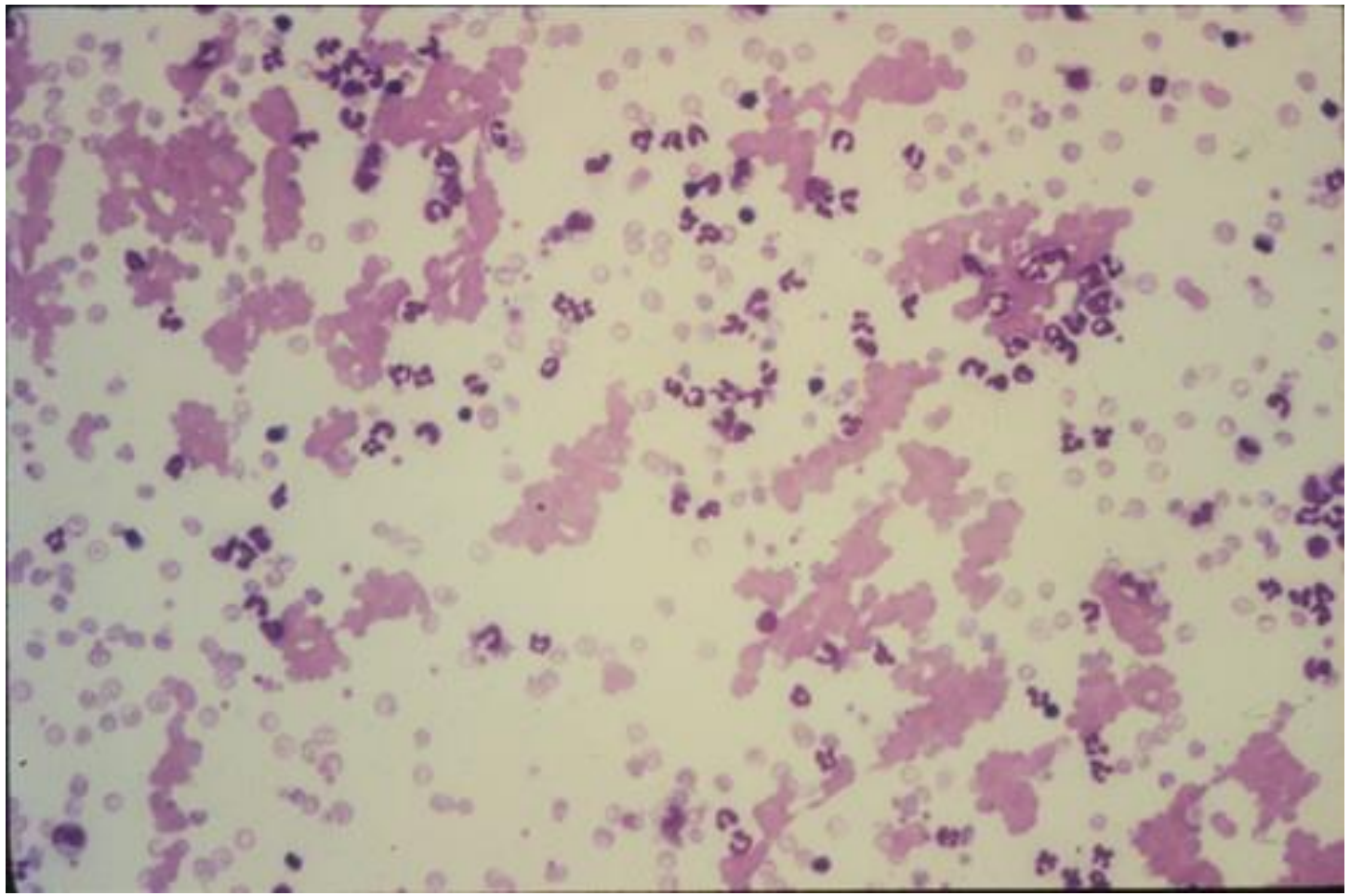
Figure 3.7. Agglutination. There are several irregular clusters of red blood cells present; this is agglutination. These are present throughout the field, but three large clumps are present (center). Agglutination may be seen in animals with immune-mediated anemia. Equine blood smear; 50× objective.











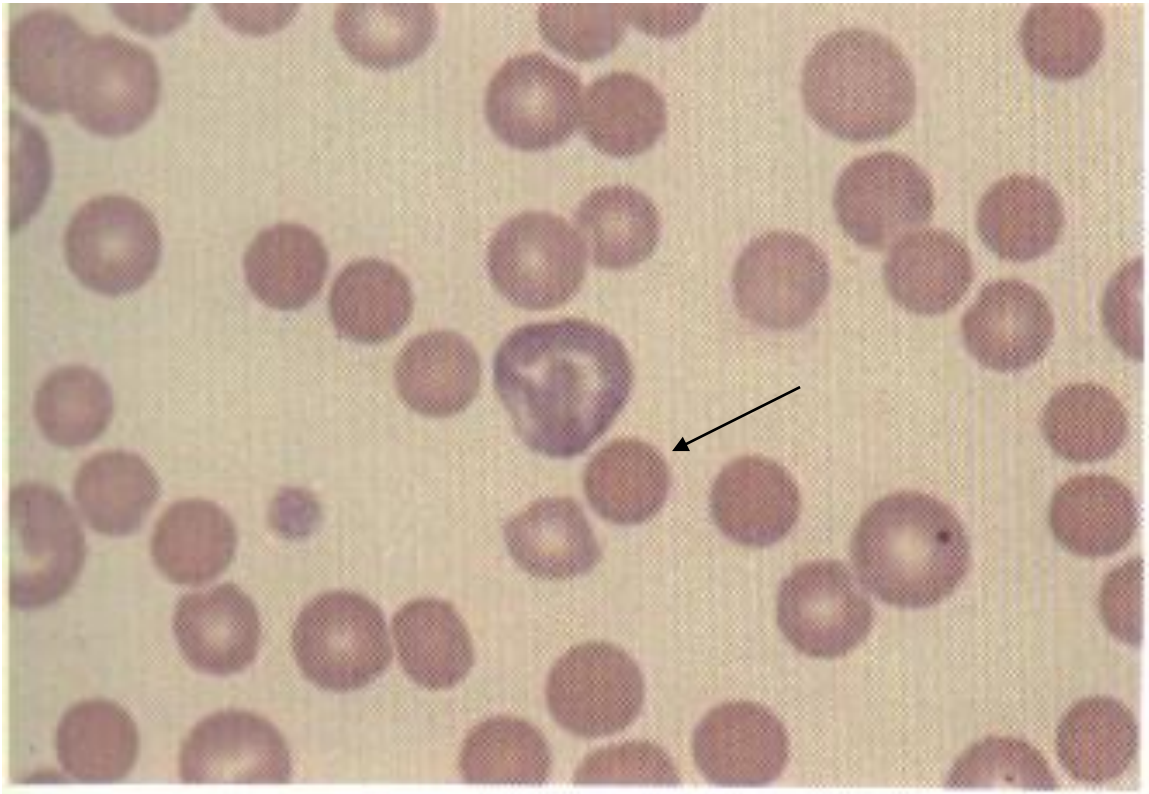
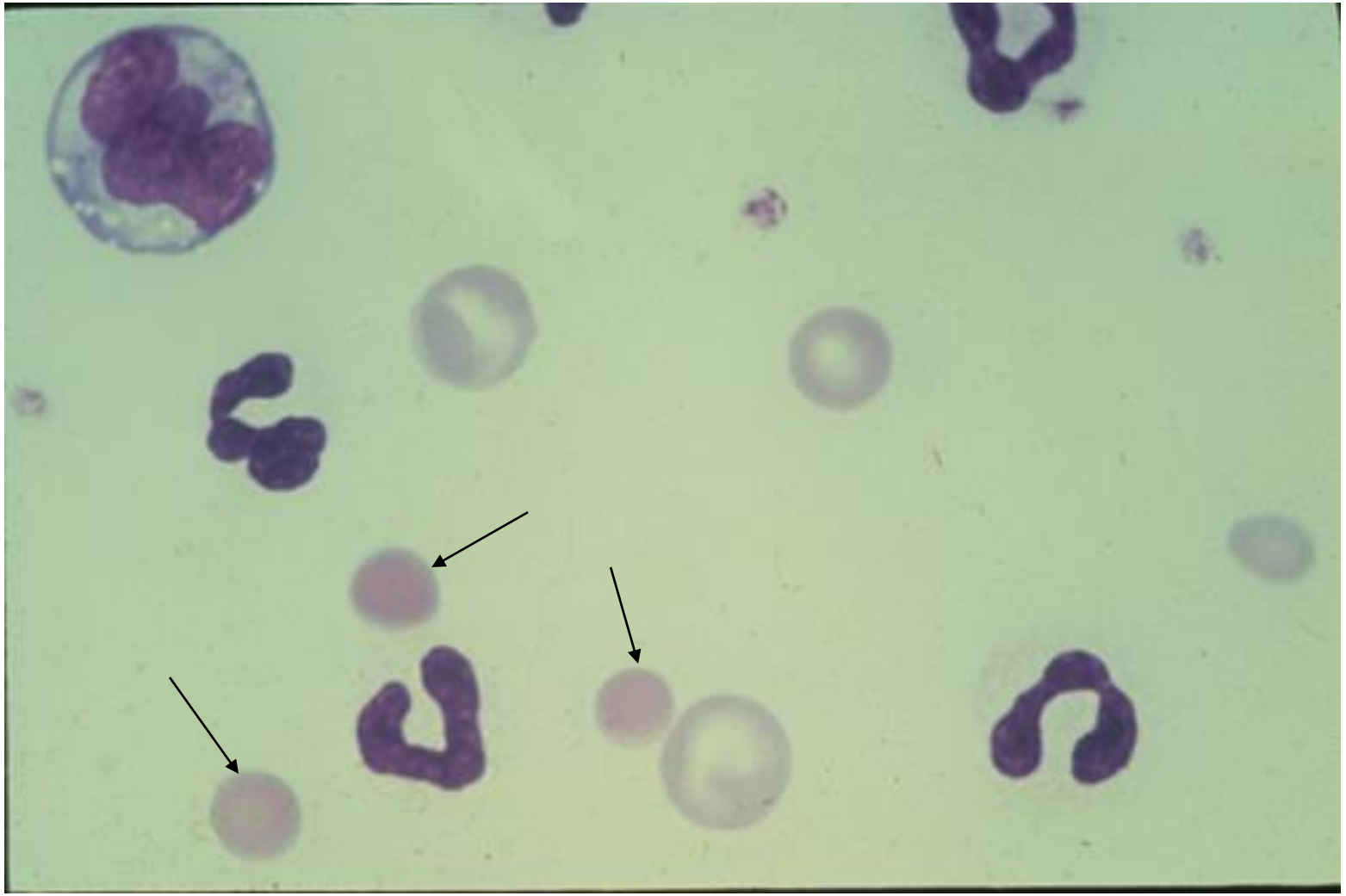


Figure 3.6. Spherocytes. The smaller cells that lack central pallor are spherocytes. These cells may be present in relatively high numbers in animals with immune-mediated hemolytic anemia. There is also a polychromatophil (center), and a red blood cell (lower right) with a Howell-Jolly body. Canine blood smear; 100× objective.



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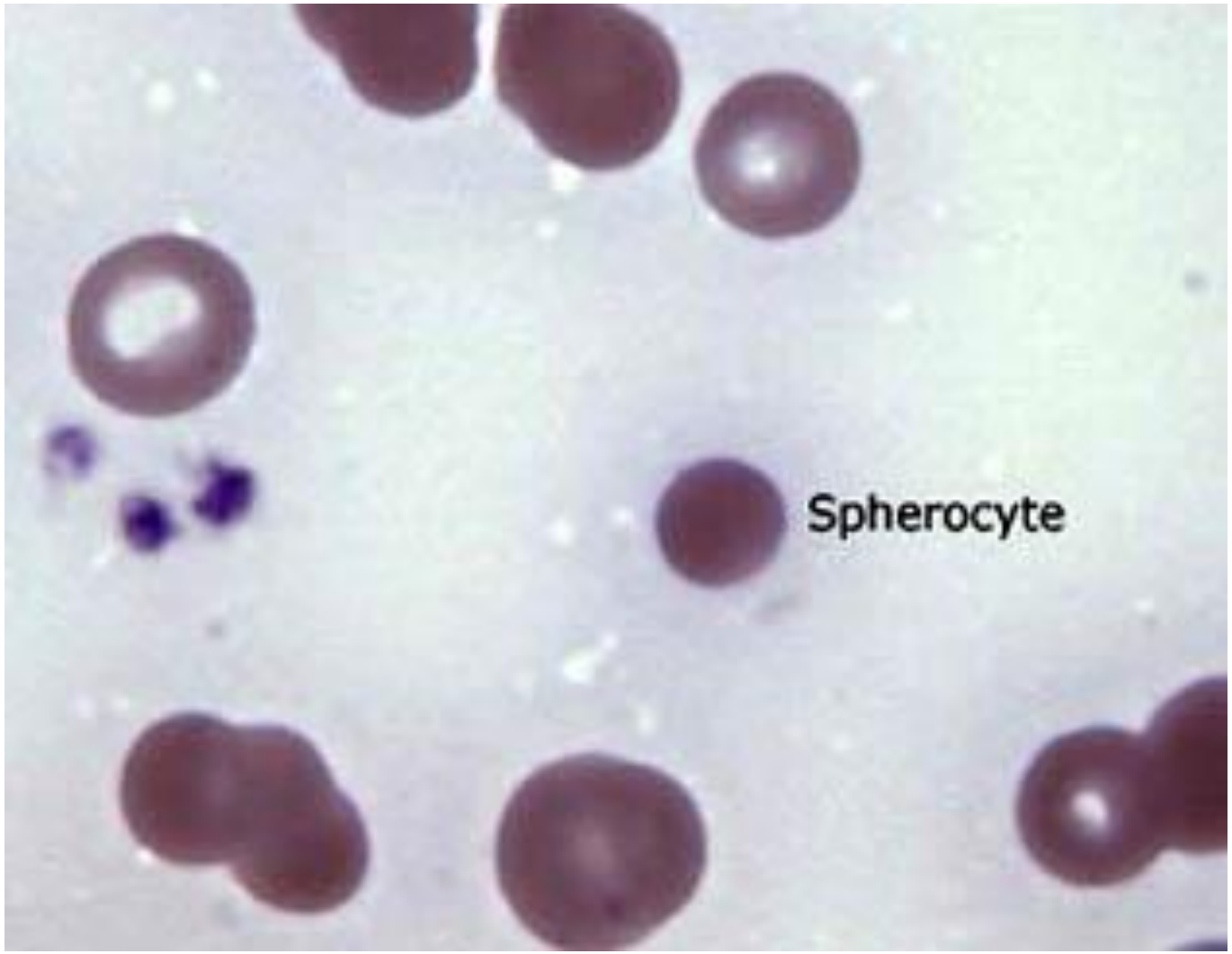


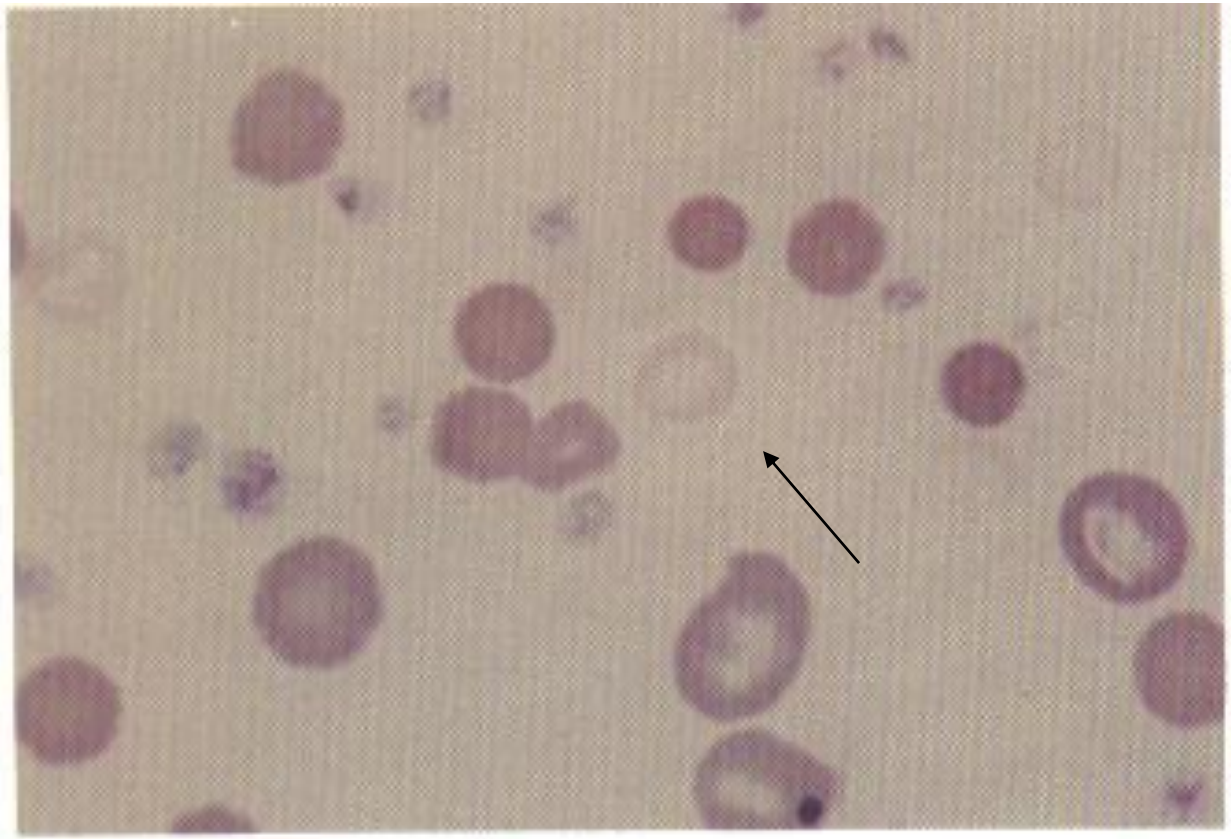
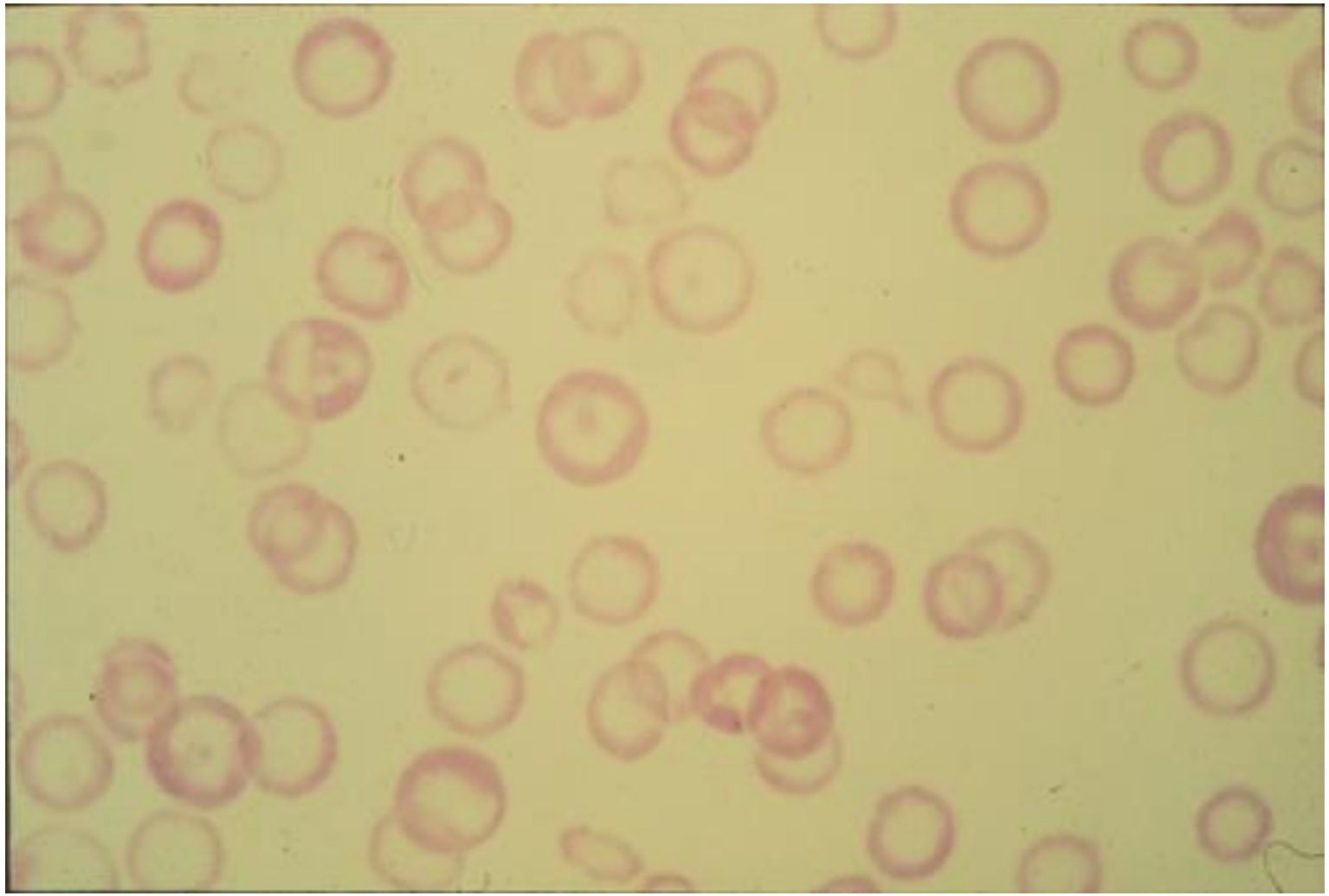


Figure 3.9. Ghost cells. The four very pale, small red blood cells are ghost cells. These indicate intravascular hemolysis. Also visible are spherocytes, polychromatophils, and a red blood cell with a large Howell-Jolly body. Canine blood smear; 100× objective.

نشان دهنده همولیز داخل عروقي است



Blood Products

- Blood products are used to treat a variety of conditions including: anemia (hemmorrage, hemolysis, coagulopathies, DIC)
- RBC products – provide the recipient with additional red cell mass to increase the O2-carrying capacity of the blood, and thus improve O2 delivery (FWB, Packed RBCs)
- Plasma products –a source of coagulation factors and various plasma proteins (FFP, SFP)

Continued…

Plasma:

- 45ml/kg will raise the albumin 1g/dL.

For clotting factor replacement estimated dosage is: 10-30ml/kg.

Note:

Clotting times should be rechecked at the end of an Fresh Frozen Plasma transfusion (FFP) to determine if more plasma is required.

Platelet Concentrate:

1 unit of platelet concentrate is derived from 1 unit of FFP. 1 unit of platelet concentrate for 10kg body weight.

Note:

The main role of platelet transfusion is to control active bleeding.

Packed Red Blood Cells (PRBC)

- Red blood cell transfusion is only administered in life-threatening situations, as the patient's immune system will also attack and destroy these RBCs as well
- However, transfusions should **never** be withheld if needed. Several transfusions may be needed before disease is under medical control
- If transfusion is necessary as a life-saving measure, only the absolute minimum number of RBCs should be administered (12ml/kg of body wt.)

- Blood component therapy permits options for smaller volume, specific replacement therapy and reduces the frequency of transfusion reactions.

Plasma

- Contains all of the clotting factor except platelets
- Indications : inherited coagulation factor deficiencies, vitamin K deficiency, DIC, severe liver disease

Platelet Rich Plasma

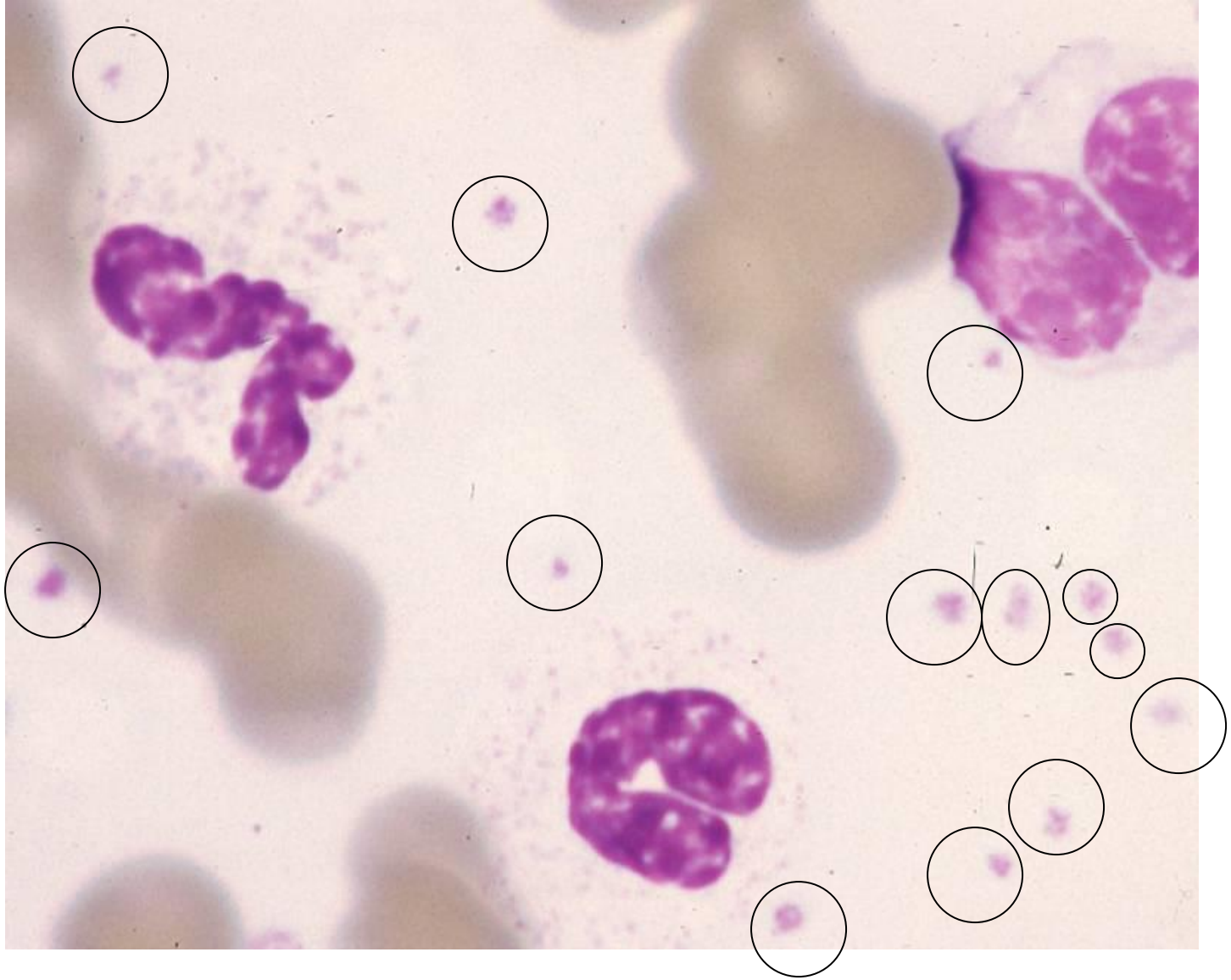
- Harvested from a unit of FWB that is less than 8 hours old and has not been cooled below 20 degrees C (68 degrees F)
- Indications : to stop severe, life-threatening bleeding in patients with thrombocytopenia

Thrombocytopenia

- Decrease of platelets in blood

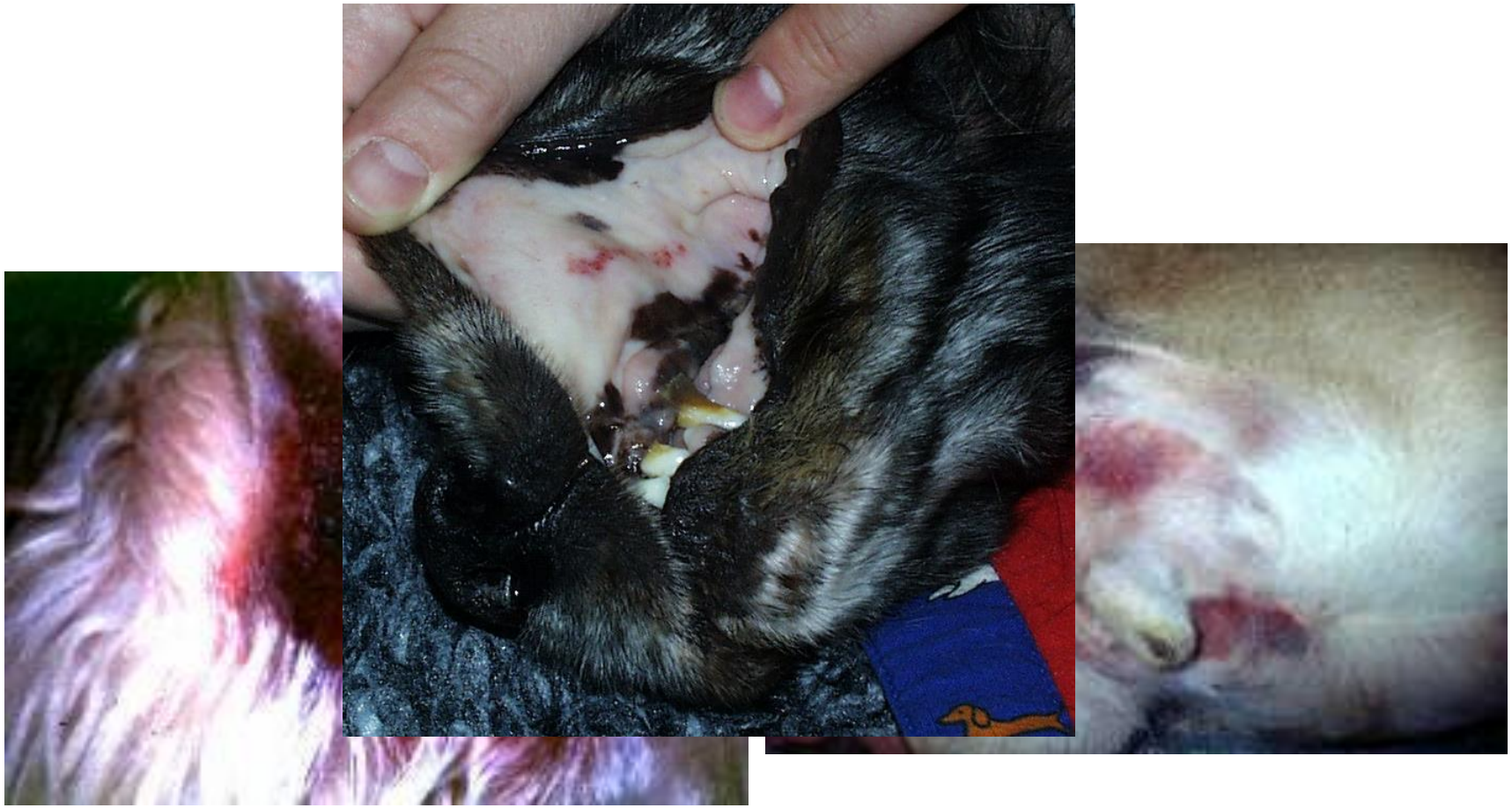
Platelets

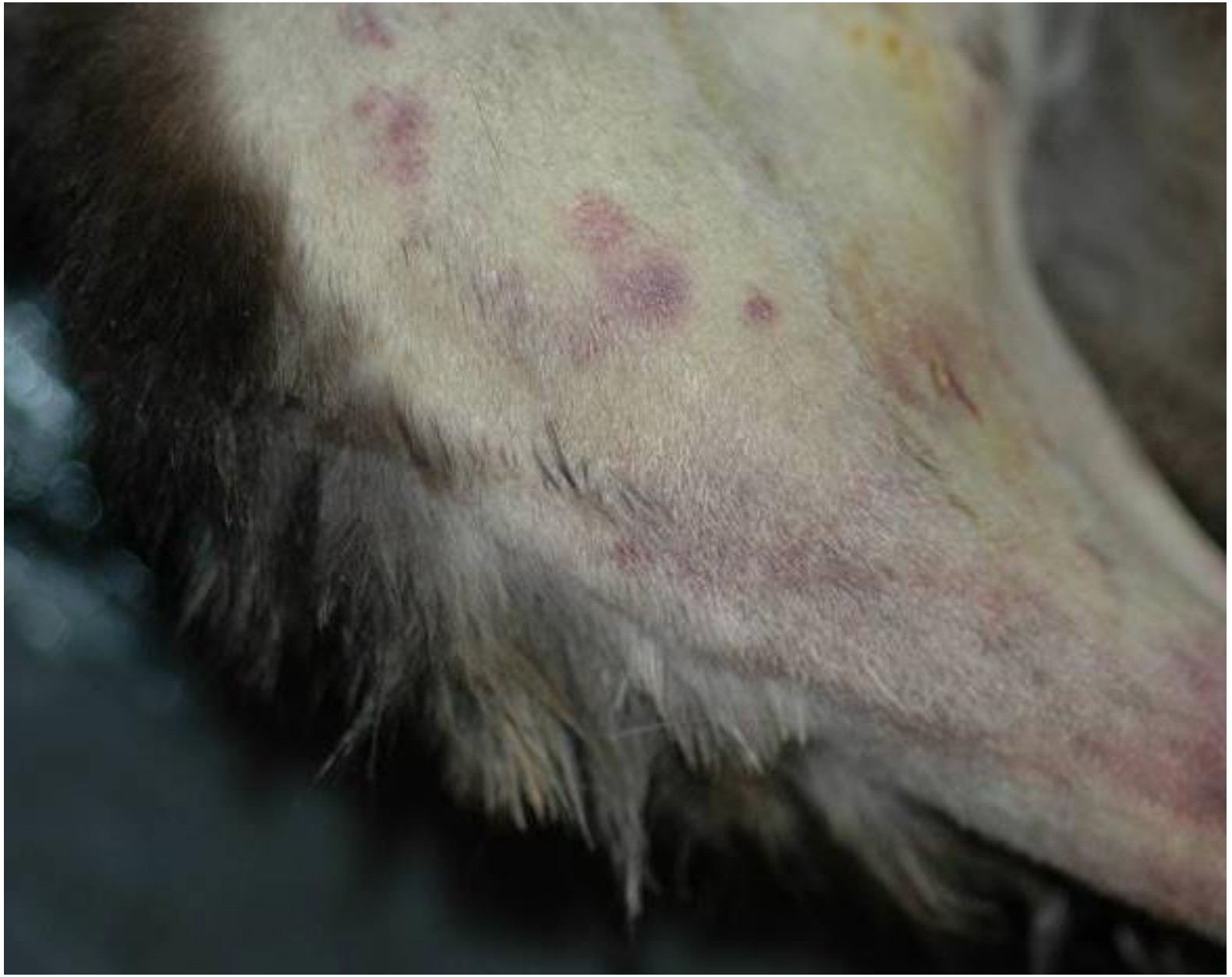
- Circulate in the blood and are involved in hemostasis (causing bleeding to stop) leading to the formation of blood clots
- Average lifespan is 5-9 days



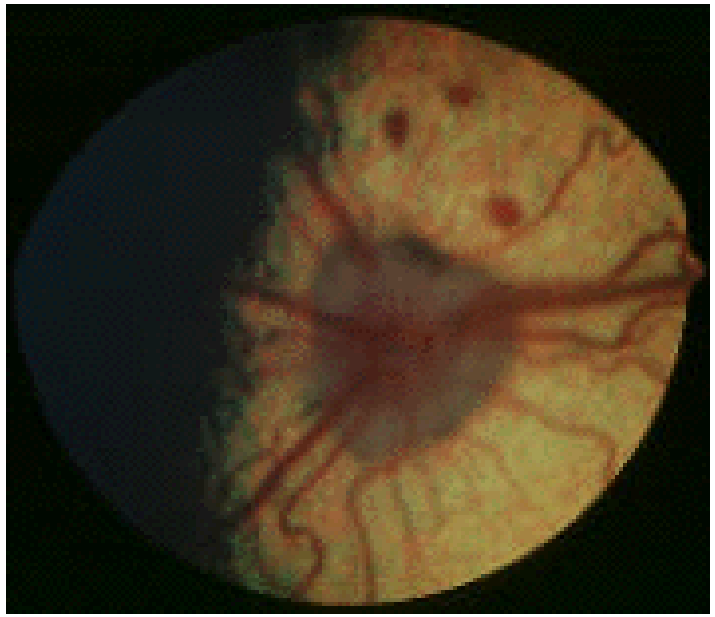
platelet

Manifestations of platelet disorders





Manifestations of platelet disorders



Whole Blood

- Initial collection called “Fresh Whole Blood” (FWB)
- Called FWB for up to 8 hours after collection
- FWB = RBCs, WBCs, platelets, plasma proteins and coagulation factors
- Builds “volume” of blood, not one specific component
- Indications : Actively bleeding animals, hypovolemia (decreased blood volume; decrease in volume of blood plasma) secondary to acute hemorrage

- The total blood volume in ml of canine and feline donors can be calculated as :

Canine = 99 x lean body weight in kg

Feline = 66 X lean body weight in kg

Generally, 10% of a donor's blood volume can be collected without causing the donor harm

Dose Calculation

Whole blood:

- 2-3ml/kg of whole blood will raise the PCV by 1%.

For Dogs:

Donor blood = 80 * Body weight * (Desired PCV- Recipient PCV/PCV transfused blood)

For Cats:

Donor blood = 60 * Body weight * (Desired PCV- Recipient PCV/PCV transfused blood)

Packed RBCs:

- 1ml/kg of PRBCs will raise the PCV 1%

The amount of blood product to be administered depends on the specific product, desired effect and patient's response. A general rule-of-thumb is that 2 ml of transfused whole blood per kg recipient weight will raise the PCV by 1%. Most patients will receive between 10 and 22 ml/kg, and a suggested formula to calculate the amount of whole blood required for transfusion in dogs is:

$$\text{volume (ml)} = 85 \times \text{bodyweight (kg)} \times \frac{\text{desired PCV} - \text{actual PCV}}{\text{donor PCV}}$$

For PRBC or FFP the average volume for infusion is 6–12 ml/kg.

The rate of administration depends on the cardiovascular status of the recipient. In general, the rate should only be 0.25–1.0 ml/kg/h for the first 20 minutes to observe for immediate transfusion reactions; if well tolerated the rate may then be increased to deliver the remaining product within 4 hours.

Leukopenia and Hypoproteinemia?

- NO
- Blood transfusions are impractical for low protein or low WBC count
- WBCs comprise such a relatively small amount of the total blood volume, it is impractical to transfuse blood in order to raise leukocyte count
- There are simpler, more practical, and less risky means available for correcting hypoproteinemia

Blood Groups

• Sheep & Goat	8
• Dog	8
• Cat	3
• Horse	9
• Chicken	11
• Cattle	12
• Pig	16

Canine Blood Types

- There are at least 19 identified canine blood groups
- They are designated by the acronym DEA (dog erythrocyte antigen) and a number
- DEA 1.1+ is the most common canine blood type
  - Dogs with this blood type are considered to be universal recipients
- DEA 1.1- or 1.2- are considered to be **universal donors**
- After the first transfusion, dogs should be blood typed and cross-matched because they can become sensitive to the type of blood that they received.

Canine Blood Types

- If a dog that has received a blood transfusion in the past becomes pregnant, it should be blood-typed, because if it is DEA 1.1 negative and received DEA 1.1 positive blood, antibodies are now present in its blood. Puppies that are DEA 1.1 positive will likely die if allowed to nurse (upon receiving antibodies to their own blood via their mother's milk)

DEA 1.1

- DEA 1.1+ is the most antigenic and is associated with most blood transfusions. It is said that about 40% or more dogs are positive for the DEA 1.1
- Dogs that are DEA 1.1 positive are universal recipients
- Breeds more commonly DEA 1.1 positive are Golden Retrievers and Labradors
- Breeds more likely to be DEA 1.1 negative, or universal donors , are Greyhounds, Boxers, Irish Wolf Hounds, German Shepherds, Dobermans, and Pit Bulls

Blood Types in dogs

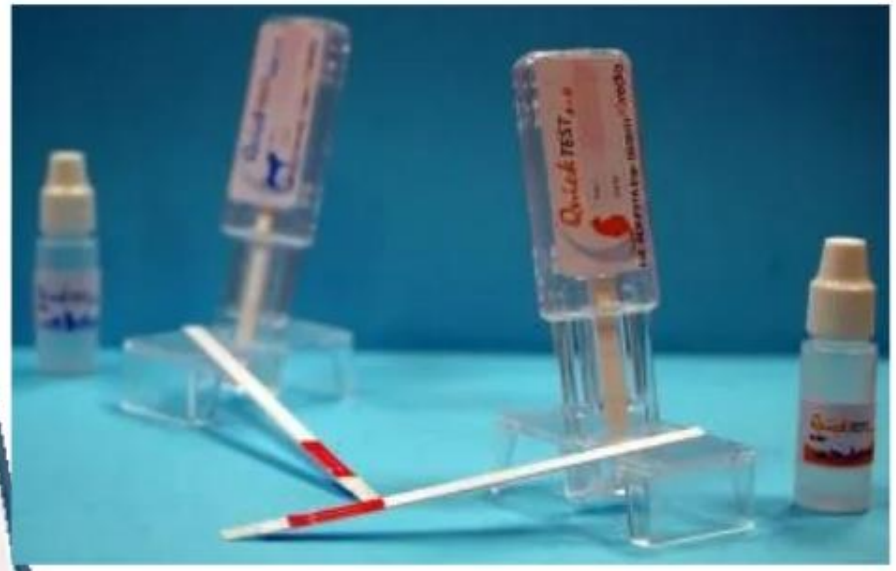
- Blood groups types are designated by the acronym DEA (dog erythrocyte antigen) and a number (DEA 1, DEA 2, DEA 3, etc). DEA 1 has two important alleles: 1.1 and 1.2. DEA 1.1-positive is the most common dog blood type

- *universal recipient* in dogs: DEA 1.1 +ve
- *Universal donor*: DEA 1.1,DEA 1.2 -ve

Blood Typing

- Identifies antigens (proteins) on the surface of RBCs
  - Positive – have the blood type antigen
  - Negative- do not have the antigen
- Many blood banking companies and blood typing labs advocate to pet owners and vet clinics that all dogs should be 'blood typed' prior to needing a transfusion to prevent sensitizing first time blood product recipients to 1.1+ antibodies
- Blood typing can be performed by using a commercially prepared blood typing card or sent to an outside laboratory
- Blood typing should be performed on each donor and recipient

Blood Typing



Canine Blood Typing

- 8 recognized DEA systems in canines.
- DEA 1.1 is considered most important
- They are either Negative or Positive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Transfusion "Freebie"

- **Alloantibodies** are naturally ocurring antibodies in the blood against the opposite blood type
- Dogs do not have alloantibodies, so the first transfusion is considered a "freebie"
- After the fist txn, however, the dog now has antibodies against the opposite blood type, so blood typing is necessary
- Humans and felines have alloantibodies, so they have to be blood typed before transfusions

Transfusion Reactions

- Examples of clinical signs associated with transfusion reactions:
  - Hemoglobinemia (presence of excessive hemoglobin in blood plasma)
  - Hemoglobinuria
  - Thrombocytopenia
  - Leukopenia
  - Pyrexia
  - Emesis
  - Incontinence
  - Urticaria (extremely pruritic wheals on skin)
  - Weakness
- Note: patients may exhibit all or a few of these symptoms

Transfusion Reactions

- With so many variations in types of blood, complete compatibility is nearly impossible. This is why crossmatching is so important
- It is also important to note that crossmatching will not identify incompatibility to DEA 1 types unless previous sensitization has occurred

Crossmatching

- Should always be performed in dogs that have received a previous transfusion
- Classified as either “major” or “minor”
- **Major crossmatching**
  - Add recipient plasma / serum to donor cells and observe for agglutination
  - Used to check for antibodies in recipient serum against RBCs from the donor
  - If **any** hemolysis or agglutination, **do not transfuse**
- **Minor crossmatching- only a concern w/ plasma txn**
  - Add donor plasma / serum to recipient RBCs
  - Checking for preformed antibodies in the donor plasma/ serum that could hemolyze recipient RBCs
  - If slight hemolysis, okay to transfuse **only RBCs**

Can my dog donate blood?

- Dogs that test negative for DEA 1.1 can give blood to dogs that are DEA 1.1 negative and DEA 1.1 positive. These dogs are considered "universal blood donors"
- Dogs that test positive for DEA 1.1 can only give blood safely to dogs that are DEA 1.1 positive
  - They can, however receive blood from dogs of any blood type and are therefore considered to be **universal recipients**

Canine Donor Requirements

- Any breed or sex may be used
- A dog with good temperament and easily accessible veins is a prime candidate
- Ideally, donors should be neutered and weigh more than 55 lb.
- Donors can be between 1 and 8 years of age
- Donors should be tested every 6 months for parasites including:
  - Heartworm (and maintained on a preventative medication)
  - Intestinal parasites

Canine Donor Requirements

- Donors should be fully vaccinated
  - Blood should not be donated for 11 to 12 days postvaccination because of vaccine effects on platelets and endothelial functions
- Donors must be in excellent health with yearly normal blood chemistry, CBC, and urinalysis
  - PCV must be at least 40%
  - Donors should also be tested for von Willebrand factor and normal platelets

Canine Donor Requirements

- Donors must be free of the following infectious diseases:
  - Blood parasites: *Babesia canis, Haemobartonella canis*
  - Rickettsial diseases: *Ehrlichia canis, E. platys, Borrelia burgodrferi,* and *Rickettsia rickettsii.*

CROSS MATCHING OF BLOOD

It detects incompatibility between donor and recipient and is essential if donor is suspected to be previously sensitized.

- **2 types of cross match are there:**

A) **Direct or Tridrop Method:**

- ❖ Take a clean glass slide.
- ❖ Put one drop of donor blood at first place; one drop of recipients blood at the second place and one drop of both donor and recipient blood at the third place.
- ❖ Mix thoroughly.
- ❖ Agglutination of third drop indicates incompatibility and the transfusion of such blood should not be carried.

Indirect or Cross reaction :

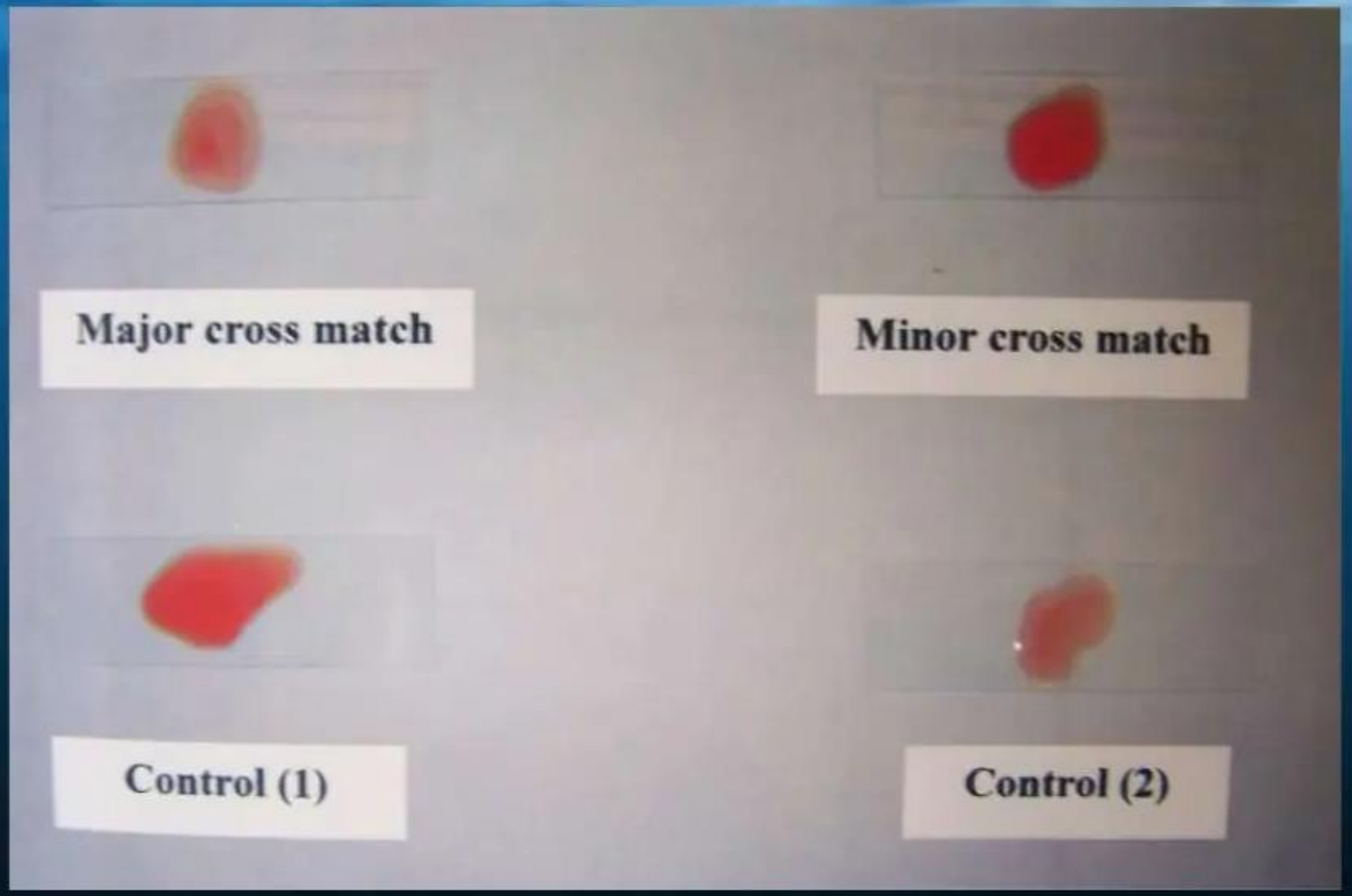
- Collect blood from both donor and recipient and allow it to clot.
- Remove the red cells, wash and resuspend in saline.

Major system of cross matching: Donor R.B.C's+ recipient serum (Confirms whether the recipient has antibodies against donor R.B.C's)

Minor system of cross matching: Recipient R.B.C's+ Donor serum (Confirms whether the donor have antibody against donor R.B.C's)

- Following incubation at 37°C, for upto one hour centrifuge the tubes and examine for evidence of incompatibility (haemolysis or agglutination of red cells).

Indirect or Cross Reaction



Dogs and Cats

Dogs and cats must have good general health and free from any disease

A minimum weight is required, Dog must weigh atleast 25 Kg and cats atleast 4.55 Kg. These weights allow 450 ml of blood to be collected from dog and 60 ml from cat without any harm to donor

Donors PCV should be atleast 40% for dogs and 35% for cats

Dogs that are to be used as regular donors must be tested for Von willbrands factor in order to ensure that platelet function is normal

Collection of Blood

- Blood can be collected from a donor every 4-6 wks.
- In large animals a safe upper limit for blood withdrawal is one litre per 200 kg body weight.
- Dogs and cats can donate 10 % of their total blood volume with no adverse effects.
- Collection of 20 % of the blood volume should not result in clinical significant anaemia but can cause hypovolumia in short term.
- When over 10 % of the donors blood volume is to be collected intravenous fluids should ideally be administered in order to prevent hypovolumia.
- The total blood volume in cats and dogs is approximately 66 ml / kg and 90 ml / kg body weight respectively.

All blood donors should have been vaccinationed as per schedule including Rabies and DHPPiL
(Distemper, Hepatitis, Leptospira, Parainfluenza, Parvo virus) for dogs and Rabies and RCP
(Rhinotracheitis, calci, panleucopenia) for cats

Blood should not be donated until 11 days, after a dog or cat is vaccinated. This is because modified live virus vaccine may affect platelet and endothelial function for upto 10 days post vaccination.

Donors should not have an infectious disease that might be transmitted through blood transfusion. Dogs must be free of bacterial and haemoprotozoal infections
(e.g. Ehrlichiosis, Borreliosis, Dirofilariasis, Trypanosomiasis, Babesiosis
Cats must be free of bacterial infections (Haemobartonellosis) , FeLV, FIV.

Canine Donor Requirements

- Donors should be fasted before donation to decrease lipemic samples of blood
- Donors should have never received a blood transfusion
- Up to 450 mL of blood can be collected from a dog once every 4 to 5 weeks

Site for collection of blood for transfusion

Animal	Site For collection
Cats	Jugular
Sheep/ Goat	Jugular
Dogs	Jugular
Horse	Jugular/ Transverse Facial vein
Cow	Jugular
Camelidae	Right jugular vein/ Cephalic

site for withdrawing blood in blood transfusion

Collection of blood

- Easiest and safest site is **jugular vein.**
- Large bore needle should be used.
- The site should always be thoroughly cleaned.
- The blood should be **rotated gently** to mix anticoagulant.

Collection of blood from cephalic vein is possible in larger breeds but less desirable as flow rate is slower and increases risk of development of microthrombi

Anti coagulants used are ACD i.e. Acid Citrate Dextrose and CPD i.e.Citrate Phosphate Dextrose

Composition of ACD
Trisodium citrate: 13 gm
Citric acid: 4.2 gm
Dextrose: 14.2 gm
D.W- 1000ml
@ 49ml/350ml of blood

Composition of CPD
Trisodium citrate: 26.5 gm
Citric acid: 3.15 gm
Sodium dihydrogen phosphate: 2.22 gm
Dextrose: 25.5 gm
D.W- 1000ml @ 75 ml/500ml of blood

Administration of blood

- Blood should be warmed slowly to room temperature before administration.
- The bags should be inverted gently several times to resuspend the red cells but should not be shaken violently.
- Cold blood should not be infused.
- Blood is given by jugular or cephalic vein.

Dose:

General dosage is : 5 – 10 ml/lb b.wt

Dosage

Based on % Hb. It is calculated as
a) 40x body weight in pounds/100=ml of blood required to raise the Hb by 1%

b) B.Wt. (kgs) X Desired PCV - PCV of Patient* /Normal PCV X K

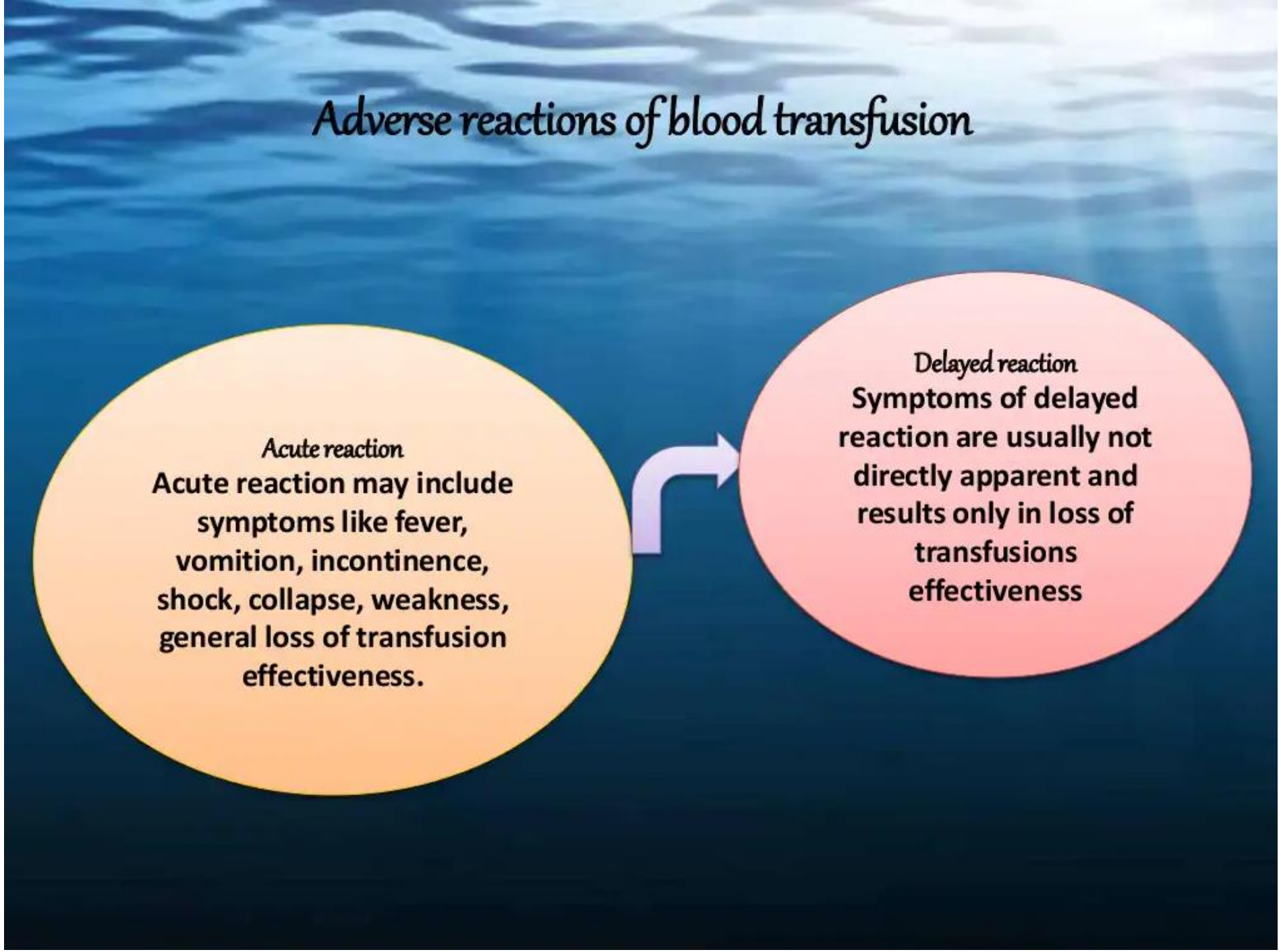
Where K=90 for dogs and 60 for cats

*Transfusion is advisable if PCV is less than 18%.

Infusion of Blood

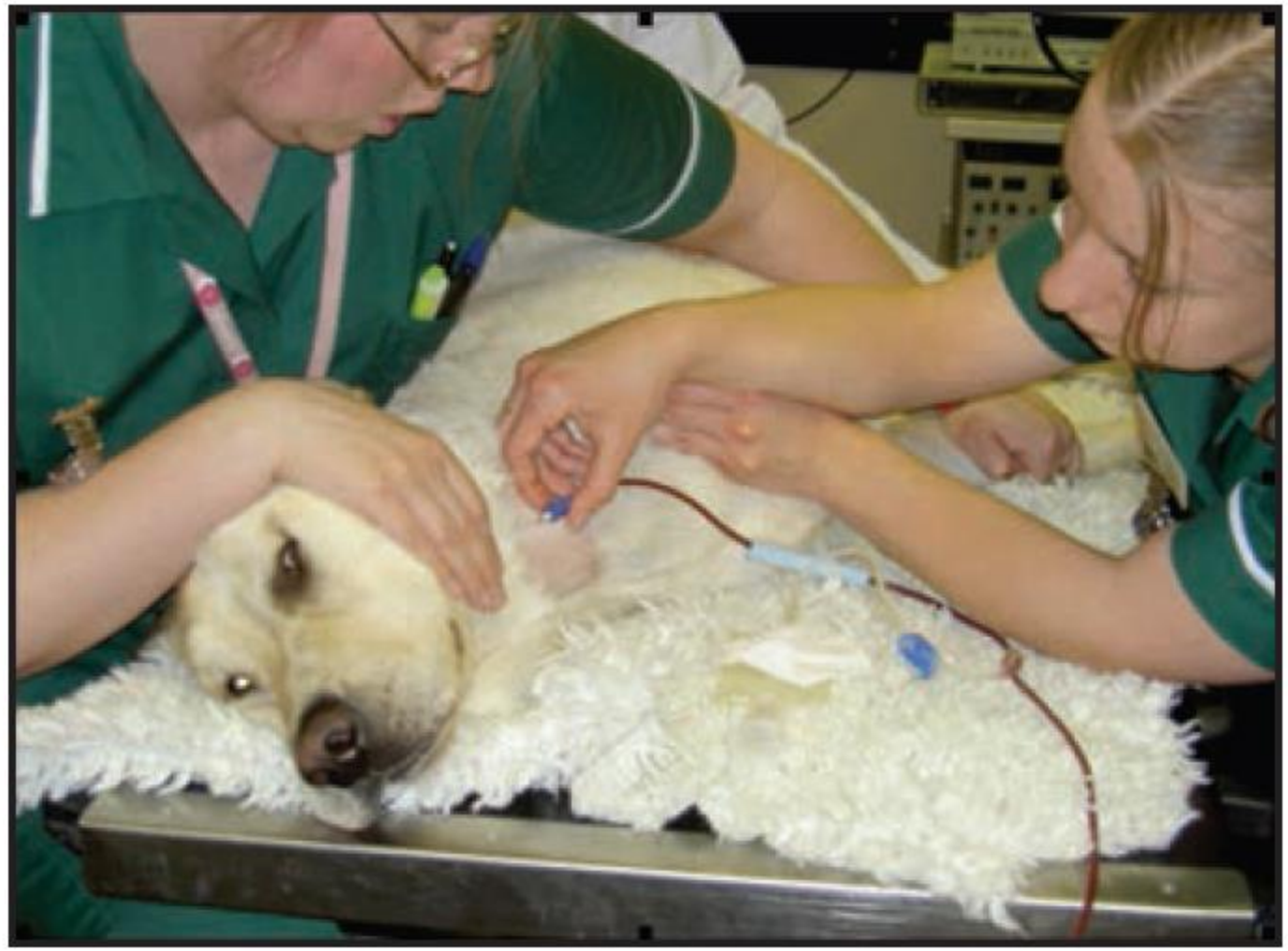
- The blood should be infused slowly (80-100 drops/min), I/V with a sterile hypodermic needle of 20 G in dogs and 18 G in cattle and horse.
- Sometimes in uncooperative animals infusion can also be carried out through intraperitoneal route, though the rate of absorption is slower compared to intravenous.
- Before administration, stored blood should be warmed to body temperature.

Adverse reactions of blood transfusion



Commercially available blood transfusion bags having cpd as anticoagulant

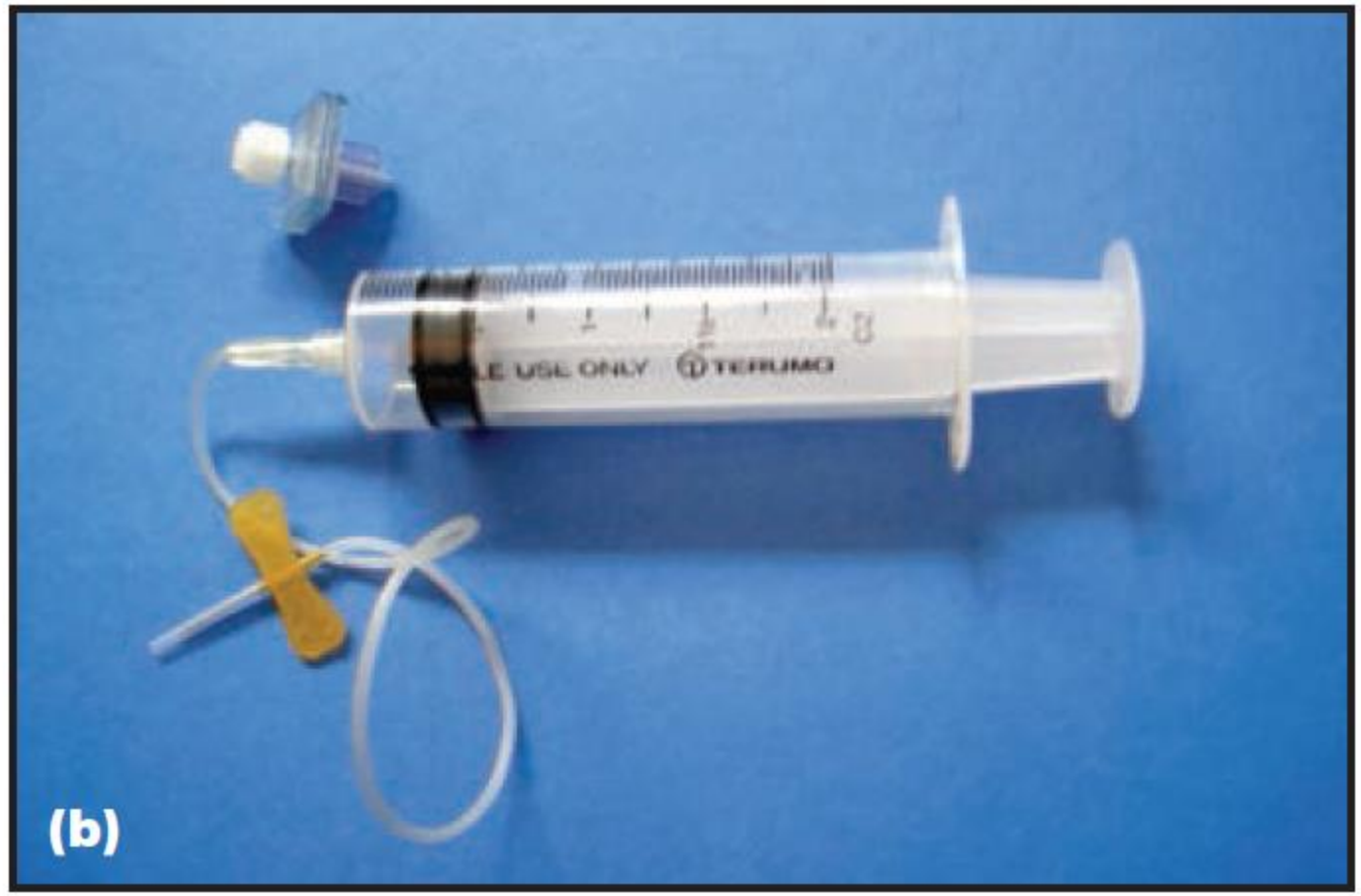
Composition of CPD
Trisodium citrate: 26.5 gm
Citric acid: 3.15 gm
Sodium dihydrogen phosphate: 2.22 gm
Dextrose: 25.5 gm
D.W- 1000ml
@ 75 ml/500ml of blood



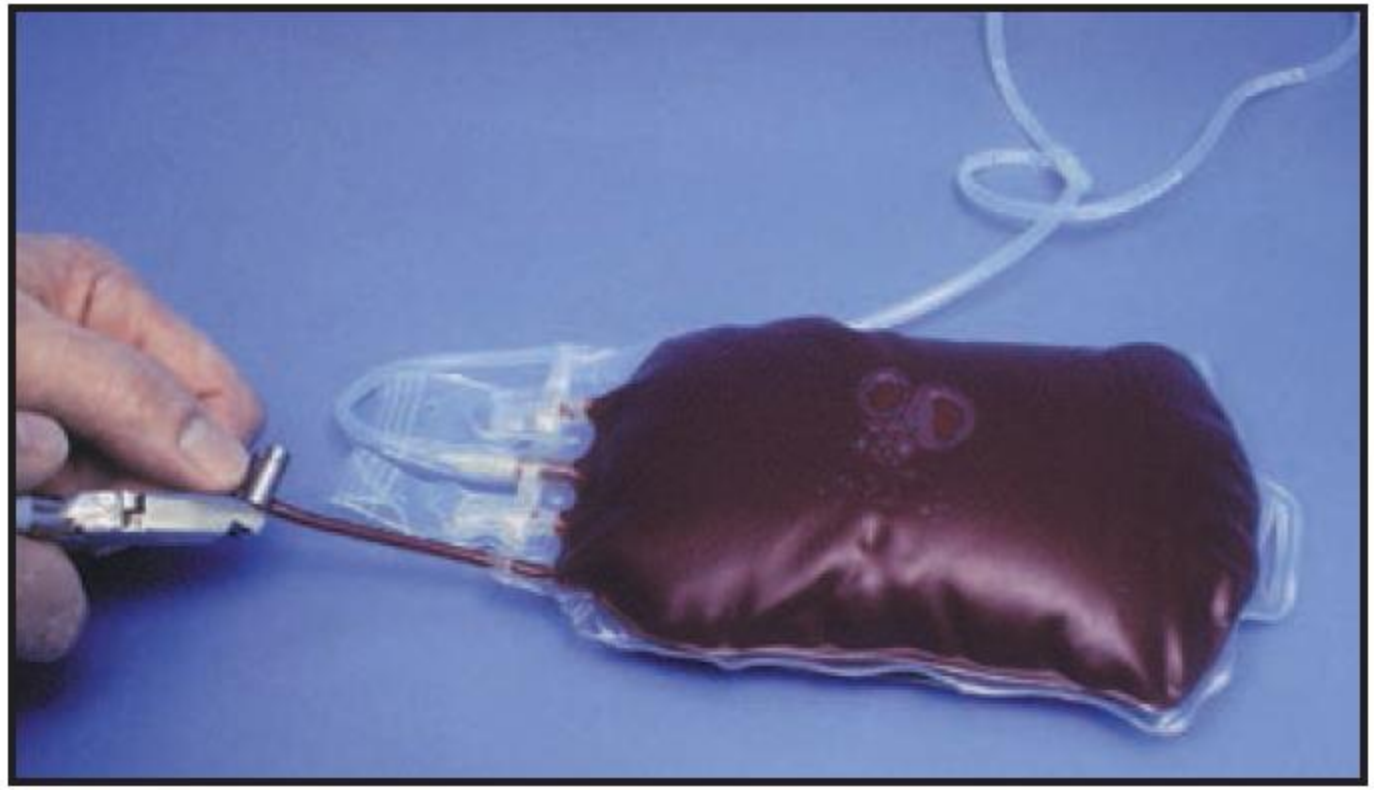
34.6 Canine blood donor in lateral recumbency.

The volume of anticoagulant used and the duration of time for which the blood product can be stored depend on the composition of the anticoagulant, the collection method and the product type. For whole blood collection ACD is used at a ratio of 1 ml anticoagulant to 7–9 ml of blood, and CPD and CPDA-1 are usually used in ratio of 1 ml anticoagulant to 7 ml of blood. Whole blood in CPD or CPDA-1 may be stored for 21 or 28 days respectively (Wardrop *et al*., 1994; Callan, 2000).

commercially available collection bags (from human and veterinary medical suppliers) that already contain anticoagulant and a swaged-on phlebotomy needle and are sterilized, sealed and protected in a plastic or foil overwrap (Figure 34.5a). Most of the standard human collection bag systems contain one or multiple bags (for component processing) to collect 450 ml into 63 ml of citrate–phosphate–dextrose (CPD), citrate–phosphate–dextrose–adenine-1 (CPDA-1), or similar anticoagulant–preservative solution, using a 16 gauge needle. The volume of blood that may be collected safely from canine donors is approximately 20% of their blood volume, every 3–4 weeks. A recommended upper volume collection limit is 18 ml/kg for dogs, and extension of the donor interval to every 8 weeks avoids the need for iron supplementation. For this reason, to ensure the safety of the donor when collecting this volume of blood, the standard human collection systems are most often used for canine donors weighing more than 25 kg.


(b)

- If blood collected into open systems is processed into components, these components must be used within 4 hours, or refrigerated and used within 24 hours of collection.

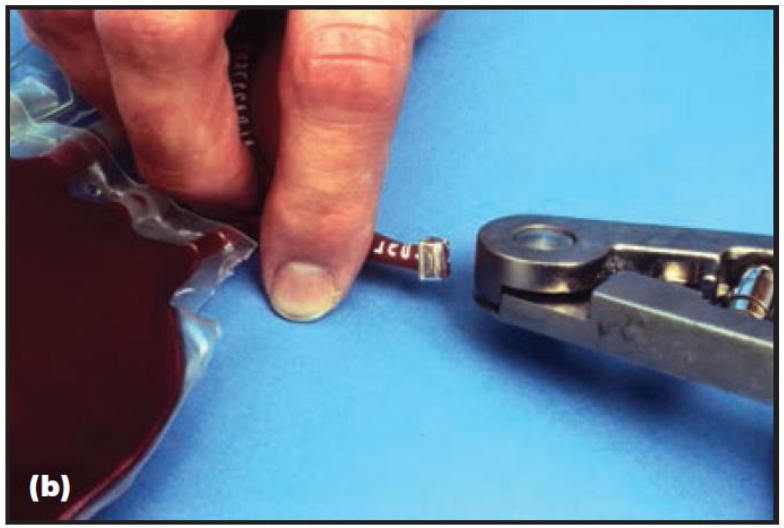


34.8 Upon completion of the transfusion, any blood remaining in the tubing is stripped into the bag.

Stored whole blood

Fresh whole blood not used within 8 hours of collection may be stored in a refrigerator at 1–6°C for approximately 21–28 days, depending on the anticoagulant–preservative used.

- The unit is then classified as stored whole blood (SWB), which will differ only from FWB by the functional reduction of labile clotting factors and platelets. When available, SWB may be useful in anaemic animals with concurrent hypoproteinaemia or loss of circulating blood volume due to haemorrhage.



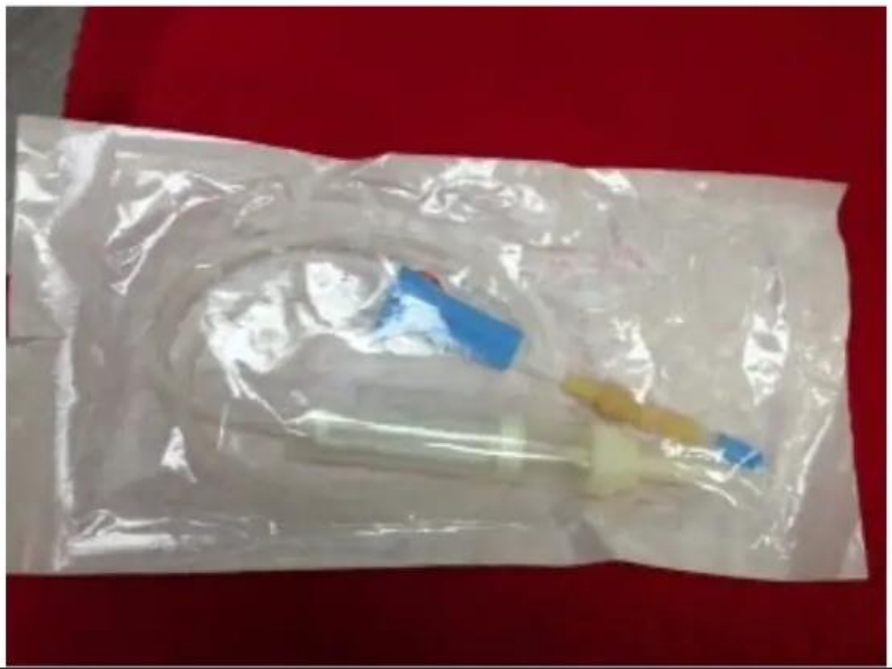
34.9 **(a)** Segments of tubing 10 cm long (marked by 'X' on the tubing) are made for later use as cross-match segments. **(b)** Aluminium sealer clips are most cost-efficient for the quantity of blood bags processed by most veterinary clinics. **(c)** Thermal sealers are more time efficient when large quantities of blood are being processed. If a sealing system is not available, firm knots may be tied, but these do not provide as secure a barrier against leakage and contamination.

Transfusion Set-up

- Hemo-nate filters

Transfusion Set-up

- Blood Set

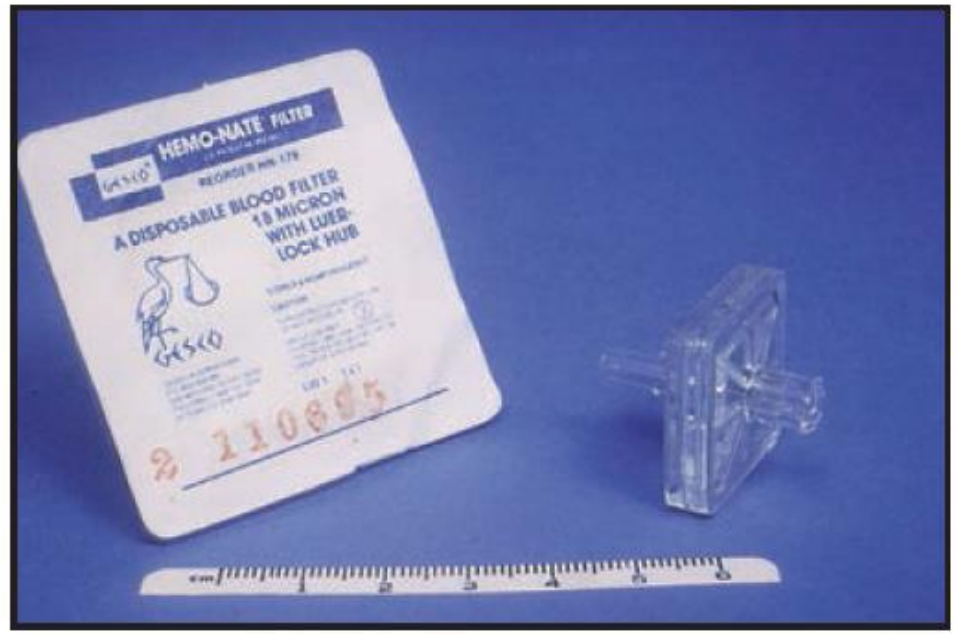


Transfusion Set-up

- Blood Set

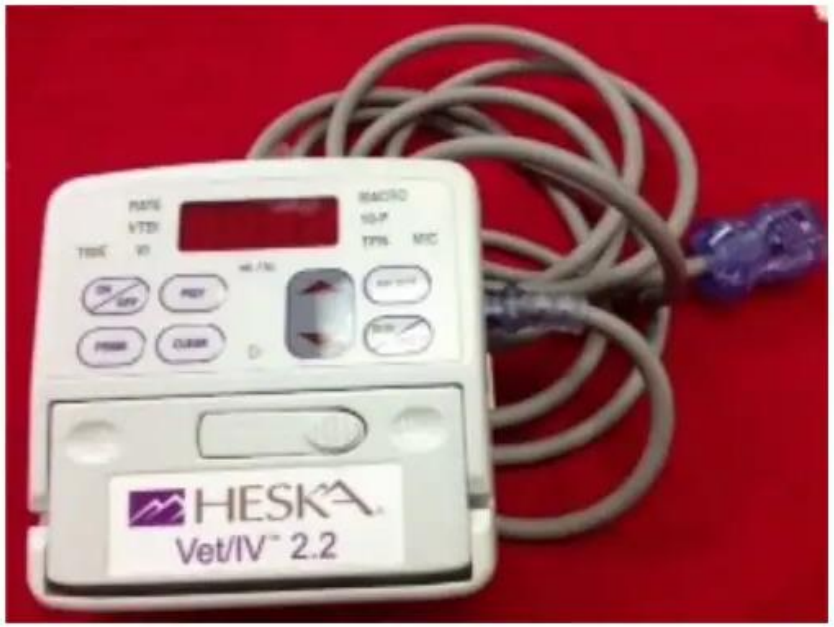
Equipment

An in-line blood filter (170–260 µm) is required for all blood products (including plasma) and is incorporated in standard blood infusion sets. A paediatric filter with reduced dead space (Figure 34.13) or microaggregate filters of 18–40 µm are useful for infusing smaller volumes of products and blood collected in syringes. The purpose of the in-line filter is to eliminate blood clots and other large cellular particles that could produce emboli in the recipient.



34.13 Paediatric filter used for administration of small volumes of blood products.

Transfusion Set-up




شهرآرا نیو


SHAHRARA NEWS


AHRARA NEWS
JMS

Packed red blood cells

- PRBC units without added nutrient solution should be re-suspended or co-administered with 100 ml of physiological saline to reduce the viscosity and improve the flow of the red cell solution.


SHAHRARA NEWS
B +
POSITIVE
4:05
5:43

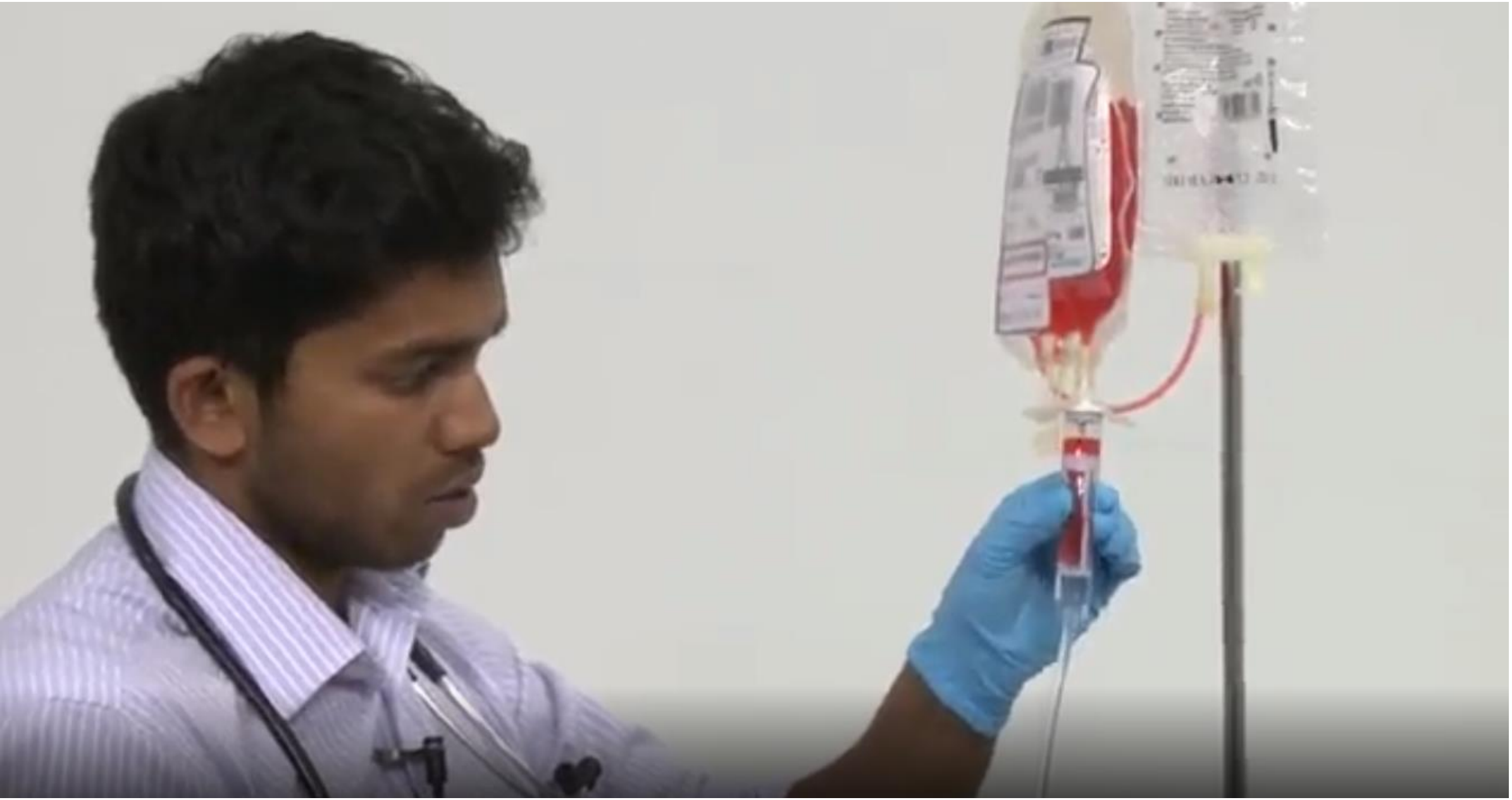
- **Fresh frozen plasma**
- Fresh frozen plasma (FFP) is separated from PRBCs and frozen within 8 hours of collection, according to human blood-banking standards. FFP provides maximum quantities of the labile coagulation factors (F) V and VIII and von Willebrand factor, as well as all other coagulation factors and plasma proteins.

- FFP is indicated for use in animals with acquired or inherited coagulopathies (inherited factor deficiencies, vitamin K deficiency or antagonism, disseminated intravascular coagulation (DIC), severe liver disease), and may be used prophylactically in patients with known coagulopathies, either perioperatively or at the time of active bleeding.

- As FFP contains other plasma proteins, it may be used in animals with hypoproteinaemia; however, large volumes and repeated transfusions are required to produce a clinically significant and sustained improvement. FFP may be stored for up to 1 year when frozen below –20°C.

Stored frozen plasma

- Stored frozen plasma (SFP) is FFP > 1 year of age, plasma not frozen quickly enough to fully protect labile factors, or FFP that has been thawed and refrozen without opening the bag. Some loss of clotting factors and anti-inflammatory proteins will have occurred, however SFP can be used for colloidal support (in hypoproteinaemia) and still provides vitamin K-dependent factors (which are not labile) to treat vitamin K deficiency or vitamin K antagonist poisoning. SFP may be stored frozen at –20°C for 5 years from the date of collection.




37.4


کاهش
فشار خون
تنگی
نفس
تب
کهیر

If the blood is for immediate use

- Di-sodium Ethylene Diamino Tetra Acetate (Na_2EDTA) @ 100mg in 10ml distilled water/500ml blood.
- Sodium Citrate as 3.8% solution @50ml/500ml blood.
- Heparin as 1% solution @ 50 ml/500ml blood.

Effect of temperature

- Blood products should be warmed slowly to body temperature before administering to prevent hypothermia and reduce vasoconstriction.
- Do not thaw plasma in boiling water or microwave and this will coagulate plasma protein.
- In urgent situation a bag of blood can be pulled from the refrigerator and given at a rapid rate as long as the blood in the IV-line is warmed by going through some form of warm water bath.

Administration Rate

It depends upon:

- Anemic status of animal.
- Age of animal.
- Health status of animal.

- In normovolemic patients at the rate of 5-10ml/kg/hr.
- In severely hypovolemic patients upto 20ml/kg/hr.
- In compromised patients (cardiac or renal compromised) can be decreased upto 2ml/kg/hr.
- Blood is administered slowly over first 30min (0.25ml/kg) and remainder within 1-4hr.
- In emergency situation such as hemorrhagic shock blood can be administered as rapidly as deemed necessory.
- Blood should never be infused over a period longer than 4hr.

Do not give blood concurrently with fluids containing calcium or hypotonic fluid as these substances can cause to lyse.

What we will need for blood transfusion

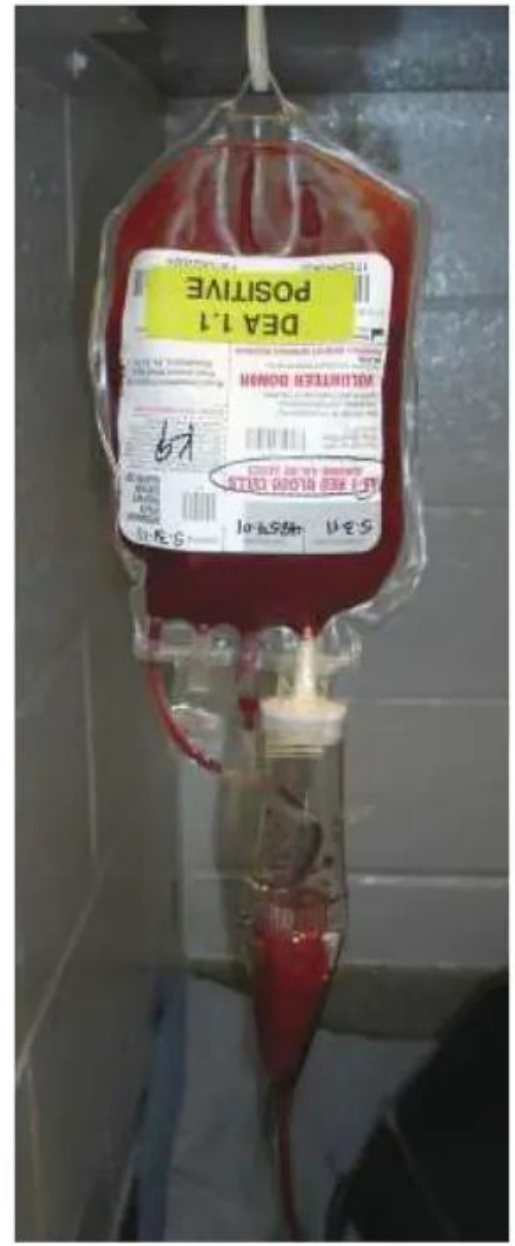
- Blood unit/Blood bag.
- Transfusion administration set (Blood Set).
- Transfusion monitoring table for patient’s record.
- Thermometer.
- Sphygmomanometer.
- Branulla .
- Clippers.
- Skin disinfectants.
- Gloves.
- Sterile swabs.

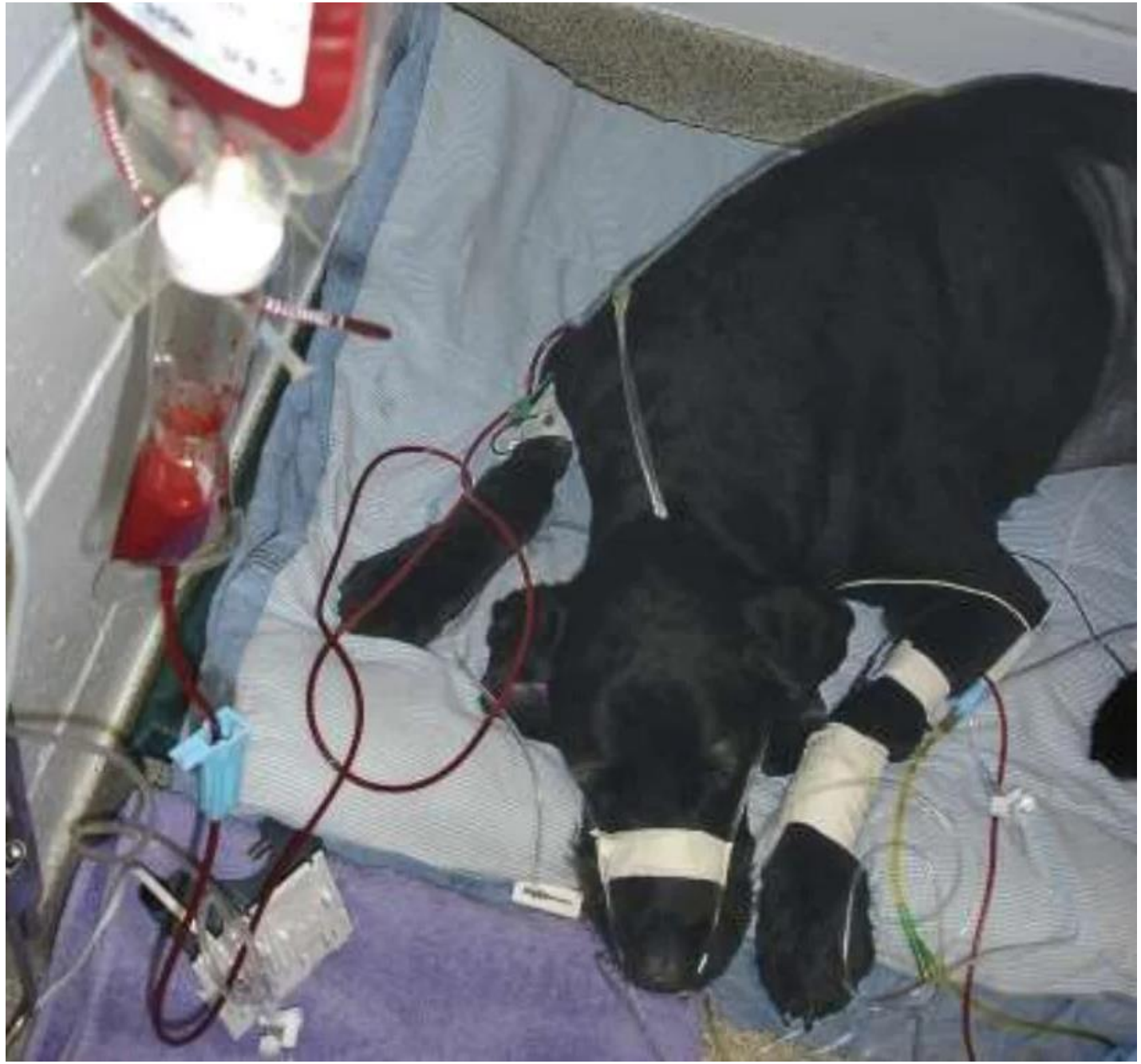
Step 1

- Verify the blood product unit size, number and expiration date as well as the donor species and blood type.
- Perform a visual inspection to detect any macroscopic abnormalities in color and consistency.
- Bacteria contaminated blood often appears brown or purple because of deoxygenation, hemolysis and methemoglobin formation.
- Also evaluate the unit for the presence of clots.

Step 2

- Attach the blood transfusion administration set to the blood unit, and prime it with blood to eliminate all air. Then connect it to the patient's catheter. Smaller catheter sizes do not cause more hemolysis than larger ones but are the main factor in limiting the infusion rate, therefore use a catheter with the largest available diameter.





Step 3

- Using a Transfusion Monitoring Chart, carefully monitor physiologic parameters and adverse reactions, including fever, hypotension, urticaria, pruritus, vomiting and shivering.
- Record baseline vital signs before starting the transfusion, then for 15min for the first 45 minutes and for 30min until the end of the transfusion. The initial infusion rate should be approximately 0.25 mL/kg for the first 30 minutes, after which the rate can be increased if no reactions are seen. The entire volume should be administered within 4 hours to prevent functional loss or bacterial growth.

TRANSFUSION MONITORING CHART

	Time	Temperature	Pulse Rate	Pulse Quality	Respiratory Rate/Effort	CRT	Blood Pressure (MAP)	Mentation	Other Observations	Initials
0 min (baseline)										
15 min										
30 min										
45 min										
1 hr 15 min										
1 hr 45 min										
2 hr 15 min										
2 hr 45 min										
3 hr 15 min										

Step 4

- When the transfusion is complete, flush the infusion site with 0.9% saline before initiating other infusions or drugs.
- Saline (0.9%) is the most compatible fluid with RBC products, hypotonic solutions cause hemolysis, and calcium-containing solutions (e.g, Ringer Lactate) can overcome the anticoagulant properties of citrate and lead to clot formation.

Step 5

- Check packed cell volume (PCV) 1 to 6 hours after transfusion.
- 70% of the transfused RBCs are expected to remain in circulation. Thereafter, if fresh whole blood was used, the RBCs should have a normal lifespan (approximately 110 days in dogs,70 days in cats).The lifespan of packed RBCs depends on the age of the unit: the longer the unit has been stored, the shorter the lifespan.

Transfusion reactions

- The types of transfusion reaction recognized may be classified as immunological (haemolytic or non-haemolytic) and non-immunological, as well as acute or delayed.

Immunological transfusion reactions

- **Acute haemolytic reaction**
- The type of transfusion reaction of most concern is an acute haemolytic reaction with intravascular haemolysis. This is an antigen–antibody, type II hypersensitivity reaction, primarily mediated by IgG.
- This type of reaction is seen in DEA 1.1-negative dogs sensitized to DEA 1.1 upon repeated exposureas well as other sensitized alloantibody-mediated incompatibilities. Clinical signs may include fever, tachycardia, dyspnoea, muscle tremors, vomiting, weakness, collapse, haemoglobinaemia and haemoglobinuria. These reactions may lead to shock, and uncommonly DIC and renal damage.

- Acute febrile non-haemolytic transfusion reactions and reactions to bacteria-contaminated blood products may have similar signs to acute haemolytic reactions.

Non-haemolytic reactions

Non-haemolytic immunological reactions are those of acute type I hypersensitivity reactions (allergic or anaphylactic), most often mediated by IgE and mast cells. These patients show a range of clinical signs from urticaria to pulmonary oedema, which may include pruritus, erythema, oedema, vomiting and dyspnoea. If this type of reaction occurs, the transfusion should be stopped and the patient examined for evidence of haemolysis and shock. Antihistamines (diphenhydramine 1–2 mg/kg i.m. or chlorphenamine 2.5–5 mg i.m. for a small to medium-sized dog, or 5–10 mg i.m. for a medium to large dog) and steroid medication (dexamethasone 0.5–1.0 mg/kg i.v.) may be required. If the reaction subsides, the transfusion may be restarted at 25–50% of the previous rate. If there is evidence of anaphylactic shock, adrenaline, intravenous fluids, antihistamines, H2 blockers (e.g. cimetidine, ranitidine), colloids, dopamine and aminophylline may also be administered at standard dosages as needed, in addition to the above treatment measures.

Reactions to leucocytes and platelets may occur, manifested by a febrile non-haemolytic transfusion reaction, which may last up to 20 hours post

transfusion. These are recognized as an increase in body temperature by > 1°C without an obvious underlying cause. The risk of these types of reaction may be minimized by the use of leucocyte reduction filters in the preparation of blood components.

Complications

- **Immediate transfusion reactions**

1. Immune mediated:

a. Hemolytic transfusion reaction
b. Febrile reaction
c. Urticarial reaction
d. Noncardiogenic pulmonary edema

2. Non-immune mediated:

a. Sepsis
b. Circulatory overload
c. Citrate toxicity
d. Hemolysis
e. Hyperammonemia

Complications

- **Delayed transfusion reactions**

1. Delayed immune transfusion reactions
2. Infectious disease transfusion

Reaction and its treatment

- Hiccups, dyspnoea, weak pulse, shivering, sweating, increased salivation, frequent micturition and defecation etc.
- Transfusion of large volume of blood may cause citrate toxicity resulting in hypocalcemia which can be treated by administering calcium borogluconate.
- Similarly transfusion at a too faster rate may cause acute heart failure.
- These reactions respond well with an early attempt and large doses of :

- Adrenaline (1:1000) @ 5-8ml/IM
- Corticosteroids @3-5ml I/V
- Chlorphenaramine maleate @5-10 ml I/M

Use of Blood Products

A) Plasma:

- Indicated in hypoproteinemia or hypovolaemia not caused by haemorrhage.

- It is also useful for the passive transfer of immunity to neonatal animals. If plasma is harvested fresh and frozen at once it can also be used as a source of coagulation factors and can be used to treat DIC (Disseminated Intravascular Coagulation).

B) Packed red cells:

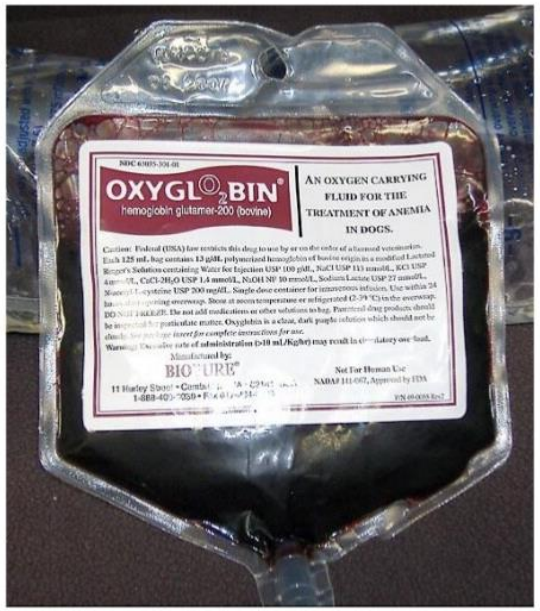
- Used for the treatment of anaemia in animals in which whole blood would cause a dangerous circulatory overload.

- To facilitate infusion, particularly in small patients, the packed red cells may be mixed with a similar volume of saline to reduce the viscosity of the fluid.

C) Platelets :

- Low speed centrifugation of fresh blood (375 g for 15 minutes) will produce a plasma supernatant rich in platelets which can be used to treat both DIC and thrombocytopenia.

Oxyglobin


OXYGLOBIN®
hemoglobin glutamer-200 (bovine)
AN OXYGEN CARRYING FLUID FOR THE TREATMENT OF ANEMIA IN DOGS.
Caution: Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.
Each 125 mL bag contains 13 g/dL polymerized hemoglobin of bovine origin in a modified Lactated Ringer's Solution containing: Water for Injection USP 100 g/dL, NaCl USP 113 mmol/L, KCl USP
CaCl-2H2O USP 1.4 mmol/L, NaOH NF 10 mmol/L, Sodium Lactate USP 27 mmol/L,
L-cysteine USP 200 mg/dL. Single dose container for intravenous infusion. Use within 24
DO NOT FREEZE. Do not add medications or other solutions to bag. Parenteral drug products should
be inspected for particulate matter. Oxyglobin is a clear, dark purple infusion which should not be
Manufactured by:
BIOPURE®
11 Hurley Street • Cambridge
1-888-469-7058 • F
Not For Human Use
NADA 141-067, Approved by FDA

Oxyglobin

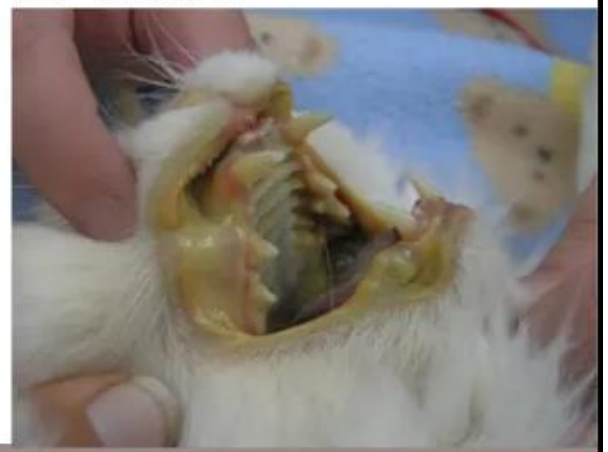
- Contraindicated in dogs with a predisposition to volume overload such as those with advanced cardiac disease or otherwise severely cardiac function or oliguria or anuria.

Oxyglobin

- Has a very minimal risk of transfusion reaction, therefore typing and crossmatching is not needed.

Oxyglobin

- Cleared quickly from the body
- Beneficial effects last only 24-36 hours
- It is a pigment and will cause yellow/red/brown discoloration of mucous membranes, sclera, urine and skin.



Oxyglobin

- Handle aseptically – great medium for bacterial growth
- No need for a blood filter
- Can use any infusion set
- Administer through a central line or peripheral vein only

Feline Blood Groups

- The AB system of blood typing is used for cats
- Blood group A is the most common in cats overall in North America
  - Nearly all DSHs and DLHs have type A blood
- Blood group B is common in European breeds (Devon rex, Abyssinian, British shorthair)
  - Many purebred cats have type B blood
- Blood group AB is rare

Feline Blood Types

- Since cats have naturally occurring alloantibodies (body gains immunity against antigens of another individual of the same species, which are perceived as foreign) against the blood-type antigen that they lack, there is **no universal feline blood donor**
- Type A cats should receive type A blood, type B cats should receive type B blood
- Type AB cats can receive either type A or type B blood with no clinical reactions

Feline Blood Types

- Cats can have severe reactions to the first transfusion due to the inheritance of preformed antibodies to the opposite blood group. Remember alloantibodies?
- ALWAYS perform blood typing and cross-matching prior to performing blood transfusion in cats

This cat is Type B

Fading Kitten Syndrome

- Kittens born to Type B mothers
- May have type A fathers so kittens may be type A, B, or AB
  - These mothers have strong anti-A antibodies titers
  - These antibodies are absorbed from the colostrum of the nursing kittens and will attack the blood cells of Type A and AB kittens causing hemolytic anemia
- These seemingly healthy kittens become ill and die unexpectedly

Indications for transfusion

- Hypovolaemia due to loss blood
- Severe anaemia with symptoms due to inadequate oxygenation of tissues
- Anaemia that cannot be corrected by bone marrow function

Feline Blood Donor Requirements

- Less than 8 years of age
- A lean body weight of no less than 10 lb.
- Donor **must be neutered**
- A good-natured indoor cat makes donation smoother and less stressful

Feline Donor Requirements

- The donor should be fully vaccinated
- Modified live vaccine may affect platelet and endothelial function, and therefore blood should not be donated for 11 to 12 days post vaccination
- Excellent health must be maintained by monitoring serum biochemistry, CBC, urinalysis, and fecal tests on a yearly basis
- The donor's PCV should be ~ 35%

Feline Donor Requirements

- All donors must be negative for feline leukemia virus, feline infectious peritonitis, feline immunodeficiency virus, and *Mycoplasma*
- A donor may provide 60 mL of blood no more than once every 4 to 5 weeks

Blood Administration

- The amount of blood product to be administered depends on the specific product, desired effect, and patient's response

10-20 ml /kg = ml of WB needed

6-10 ml / kg = ml of PRBC's needed

6-10 ml / kg = ml of Plasma needed

**Blood is transfused slowly at 1ml/kg / 15-20 min. Then rate is increased up to 22 ml / kg / hr for no more than 4 hours total

Blood Collection Procedure

- Sedation requirement depends on the animal
  - Do not use **acepromazine** because it causes hypotension
  - The sedative of choice for dogs is oxymorphone given approximately 15 to 20 minutes prior to blood collection
  - A blood collection bag with anticoagulant added or a special blood collection system can be used
  - Clippers and surgical scrub solutions are necessary for preparation of the venipuncture site
  - All supplies for IV fluid administration should also be available

Blood Collection Procedure

- Place cephalic IV catheter for fluid administration after collection
- Place animal in lateral recumbency with neck extended
- Clip a wide area around the jugular vein to be used for collection and aseptically prepare
- Insert 16-gauge needle attached to blood collection system into jugular vein and begin collection
- As blood enters bag, move bag to slightly mix with anticoagulant
- 450 mL of blood constitutes one entire blood collection for dogs; 60 mL for cats

Blood Collection

- Closed system – literally a collection bag and line with a needle pre-attached. The only exposure to air is when the needle is uncapped
- Open system – any system in which there is one or more additional site of potential bacterial contamination during blood collection or processing
  - Ex. Syringe and butterfly catheter for small volumes of blood collection

Blood Collection

- After completion of blood collection, apply pressure to jugular vein for 2 minutes to minimize hematoma formation
- The amount of blood collected from a canine donor should not exceed 10-20 mL/kg and 60 mL per cat
- Most facilities bleed a donor no more than once a month
- Clearly label collection bag with donor's name, collection and expiration dates, the donor's PCV, TP, and blood type

Blood Collection

- Multiply the volume of blood collected from the patient by three to determine the volume of replacement IV fluids
- The donor should be observed for 1 hour after donation
- Mucous membrane color, pulse, and CRT should be monitored

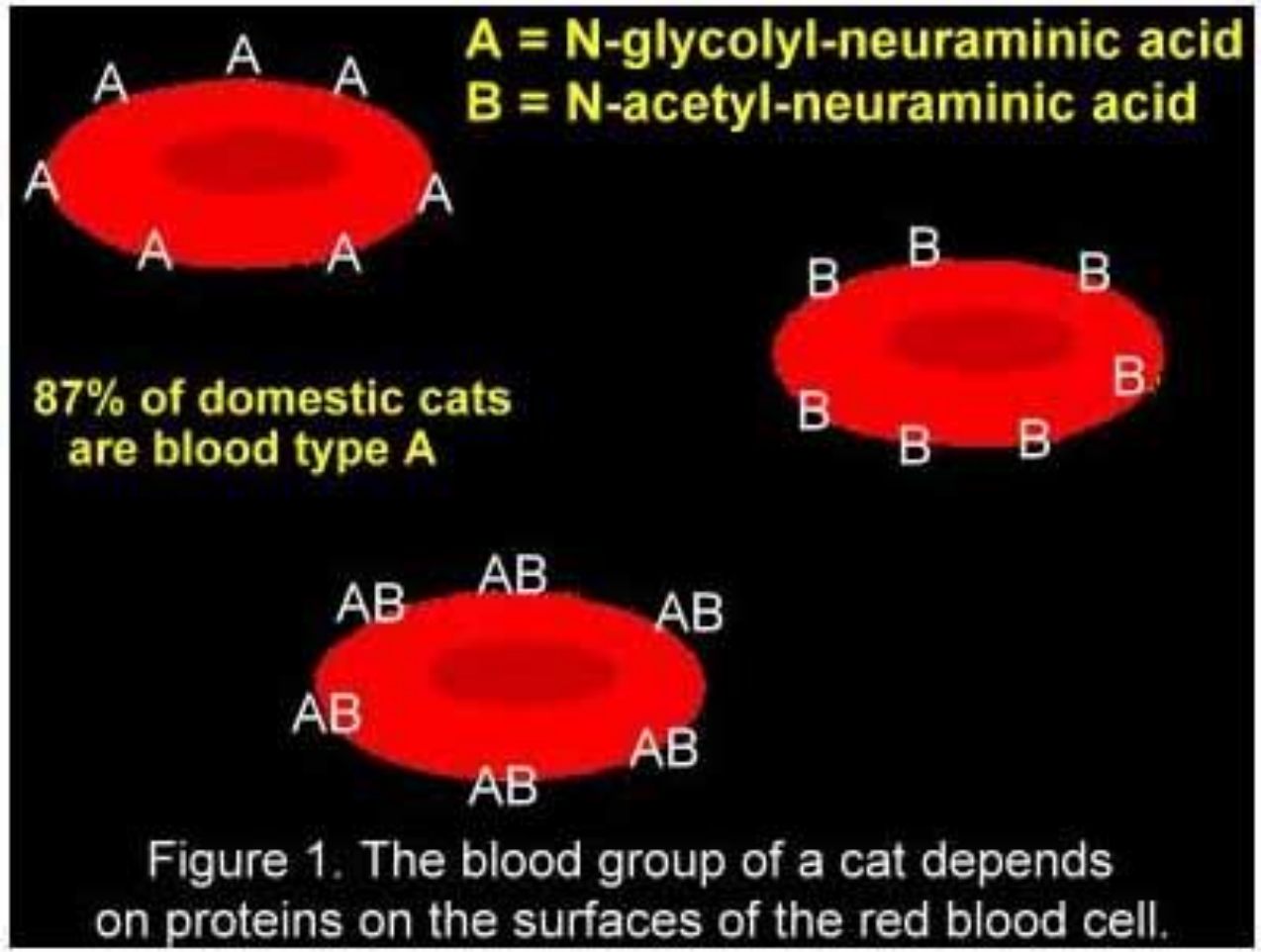
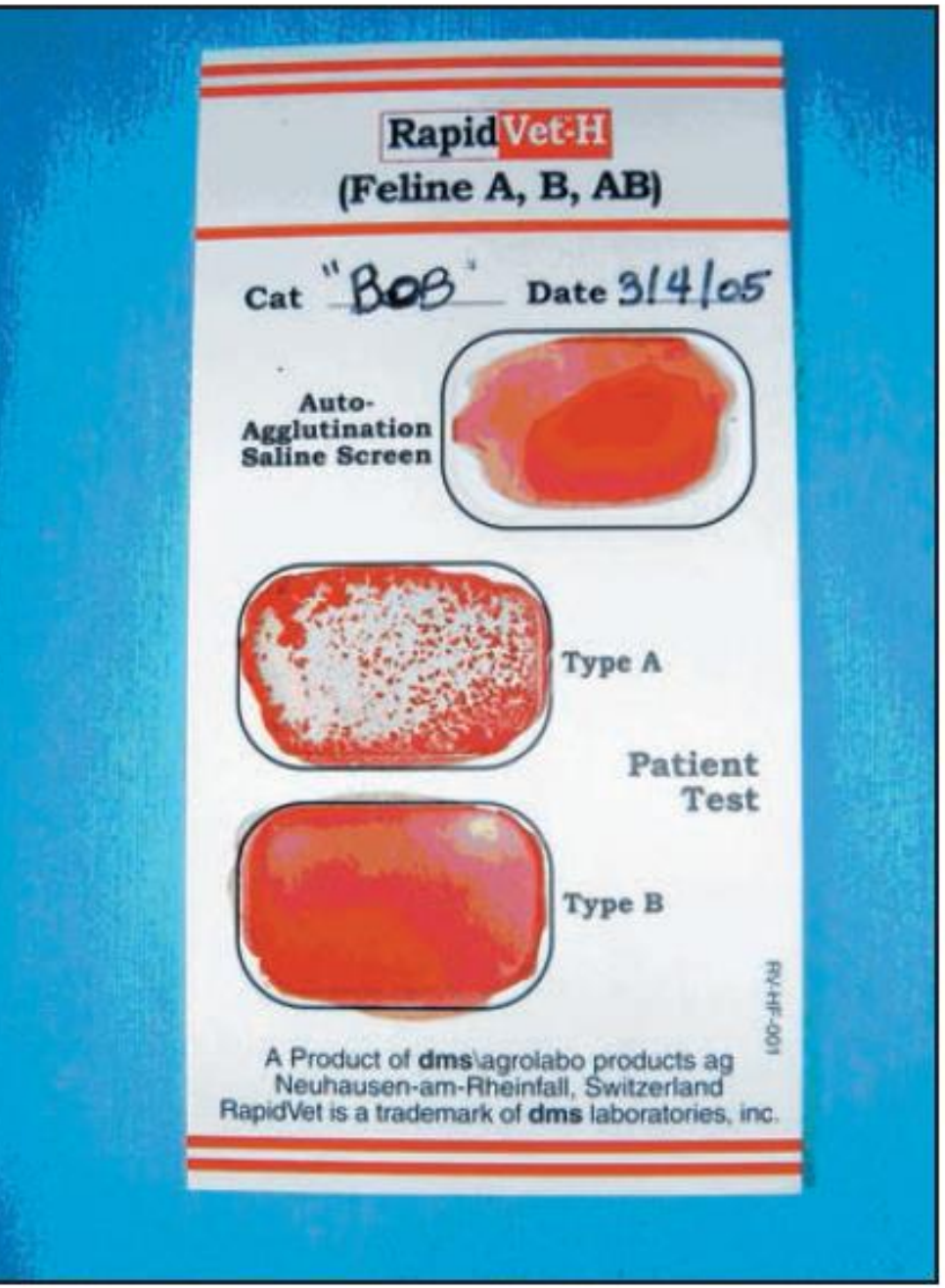
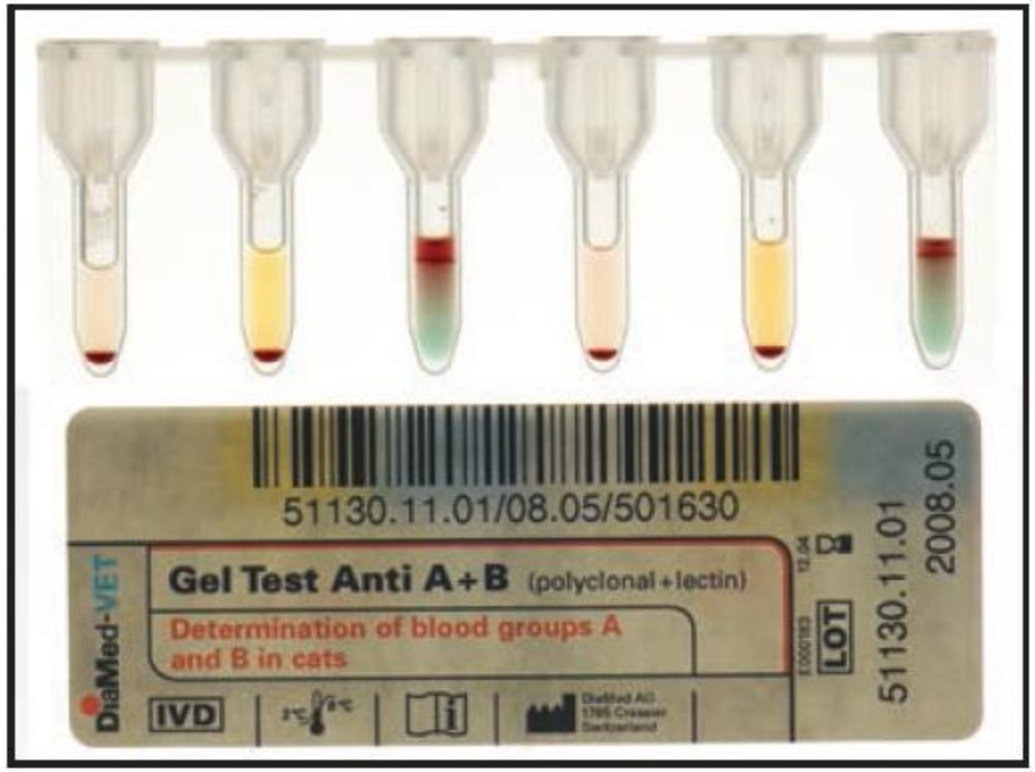


Figure 1. The blood group of a cat depends on proteins on the surfaces of the red blood cell.



33.3 The DMS Laboratories feline blood typing card. In this test the three wells in the card are first 'activated' by the addition of diluent and then patient blood is added to each. After mixing and incubation the result is determined by inspection. In this card the presence of agglutination in the anti-A well indicates that the cat is of blood group A. *(*Reproduced from *BSAVA Manual of Emergency and Critical Care).*



33.4 The DiaMed Gel Test system for feline blood typing. The six columns formed in this plastic card allow typing of two cats. From left to right the columns are negative control, B blood group antigen and A blood group antigen, and then a repeat of these for the second sample. A suspension of washed feline RBCs has been added to the reservoir above each column and the card has then been centrifuged. For both of the cats tested here, red cells have passed through the gel matrix to collect at the base of columns 1 (control) and 2 (anti-B reagent). The RBCs have collected at the top of the gel matrix in column 3 (anti-A reagent). This identifies both cats as being of blood group A.

33.5 The Alvedia Quick Test system for feline blood typing. The left-hand end of this immunochromatographic strip has been inserted previously into a suspension of feline blood cells, and these have migrated through the strip matrix to interact at specific points with typing reagents (positions B and A). A control (C) reaction is also included. This test is validated by the presence of the control line and shows that the cat is of blood type AB.

type A antigen is *N*-glycolyl-neuraminic acid (NeuGc) and the B antigen is *N*-acetyl-neuraminic acid (NeuAc). Type A cats have a dominance of NeuGc with small quantities of NeuAc, whereas type B cats have only NeuAc expression. Type AB cats have an equal amount of both molecules on the surfaces of their red blood cells (RBCs). Type B cats appear to lack the enzyme (cytidine monophospho-*N*-acetylneuraminic acid hydroxylase (CMAH)) that converts NeuAc to NeuGc.

The feline *CMAH* gene has now been sequenced and single nucleotide polymorphism (SNP) haplotypes have been associated with the A and B blood types (Bighignoli *et al.*, 2007). There are three alleles that control the AB blood type. The *A* allele is dominant over the *b* allele and the phenotype AB is the result of a third allele (a^{ab}) that allows co-dominant expression of both A and B. The a^{ab} allele is recessive to the *A* allele but dominant over the *b* allele. A cat of type A phenotype may therefore be of genotype *AA*, Aa^{ab} or *Ab.* A cat of type B phenotype must be of genotype *bb*, whereas a type AB cat may be of genotype $a^{ab}b$ or $a^{ab}a^{ab}$.

Country	Group A (%)	Group B (%)	Group AB (%)	Reference
Australia (*n* = 187)	62	36	1.6	Malik *et al.*, 2005
Brazil (*n* = 172)	94.8	2.9	2.3	Medeiros *et al.*, 2008
Germany (*n* = 372)	98.7	1.1	0.2	Weingart *et al.*, 2006
Greece	78.3	20.3	1.4	Mylonakis *et al.*, 2001
Hungary	100	0	0	Bagdi *et al.*, 2001
Portugal (*n* = 132 DSH)	90.2	3.8	6.0	Silvestre-Ferreira *et al.*, 2004
Portugal (*n* = 5 DLH)	80	6.7	13.3	Silvestre-Ferreira *et al.*, 2004
United Kingdom (*n* = 105)	67.6	30.5	1.9	Forcada *et al.*, 2007

33.1 Blood groups in Domestic Shorthair (DSH) and Domestic Longhair (DLH) cats by geographical area 2000–2009. Data prior to 2000 (including information for other countries) are reviewed in Malik *et al.*, 2005.

Breed	Group A (%)	Group B (%)	Group AB (%)	Number of cats	Country	Reference
Abyssinian	100	0	0	36	Australia	Barrs *et al.*, 2009
	89	11	0	30	Australia	Malik *et al.*, 2005
	100	0	0		Hungary	Bagdi *et al.*, 2001
Bengal	100	0	0	100	UK	Gunn-Moore *et al.*, 2009
	86	14	0	7	UK	Forcada *et al.*, 2007
Burmese	100	0	0	5	UK	Forcada *et al.*, 2007
	93	3	3	30	Australia	Malik *et al.*, 2005
Carthusian/Chartreux	77.8	18.5	3.7	27	Germany	Weingart *et al.*, 2006
Persian	80	20	0	5	UK	Forcada *et al.*, 2007
	67	22	11	9	Australia	Malik *et al.*, 2005
	100	0	0	7	Portugal	Silvestre-Ferreira *et al.*, 2004
	66.6	33.3	0		Hungary	Bagdi *et al.*, 2001
Ragdoll	80	20	0	5	Australia	Malik *et al.*, 2005
Russian Blue	80	20	0	5	Australia	Malik *et al.*, 2005
Siamese	100	0	0	13	UK	Forcada *et al.*, 2007
	100	0	0	12	Australia	Malik *et al.*, 2005
	100	0	0	19	Portugal	Silvestre-Ferreira *et al.*, 2004
	100	0	0		Hungary	Bagdi *et al.*, 2001
Somali	100	0	0	24	Australia	Barrs *et al.*, 2009
	71.4	23.8	4.8	21	Germany	Weingart *et al.*, 2006
Turkish Angora	53.6	46.4	0	28	Turkey	Arikan *et al.*, 2003
Turkish Van	42.3	57.7	0	78	Turkey	Arikan and Akkan, 2004
	40	60	0	85	Turkey	Arikan *et al.*, 2003

A new feline blood group antigen, *Mik*, has been identified recently (Weinstein *et al.*, 2007). Some type A cats lack expression of *Mik* and therefore have serum alloantibody specific for this antigen. In these cats, even an AB matched blood transfusion may potentially lead to a reaction, and so cross-matching would be required to detect this incompatibility.

Figure 2. A litter of kittens with neonatal isoerythrolysis. Note the jaundiced (yellow) noses and bloody tip of the tail of the white kitten.

Feline neonatal isoerythrolysis

Haemolytic disease of the newborn (neonatal isoerythrolysis, NI) is of clinical significance in cats (Day and Mackin, 2008). Cat breeders are very aware of this disease and will often ask to have their breeding stock blood-typed in order to calculate the risk of NI occurring in any particular mating. The disease occurs where a type B queen gives birth to type A or AB kittens and it is therefore more likely to be a problem in those breeds with a high prevalence of type B. The high concentrations of anti-A alloantibody that may be present in type B cats will be transferred in colostrum, leading to the development of classical haemolytic anaemia at around 48 hours of life. Affected kittens may have severe clinical disease characterized by jaundice, haemoglobinuria, pallor and weakness, and may die. Alternatively, there is a subclinical form of disease in which kittens may simply display tail-tip necrosis at around 3 weeks of age. These kittens will be Coombs' test-positive. NI is a major cause of the 'fading kitten syndrome'.

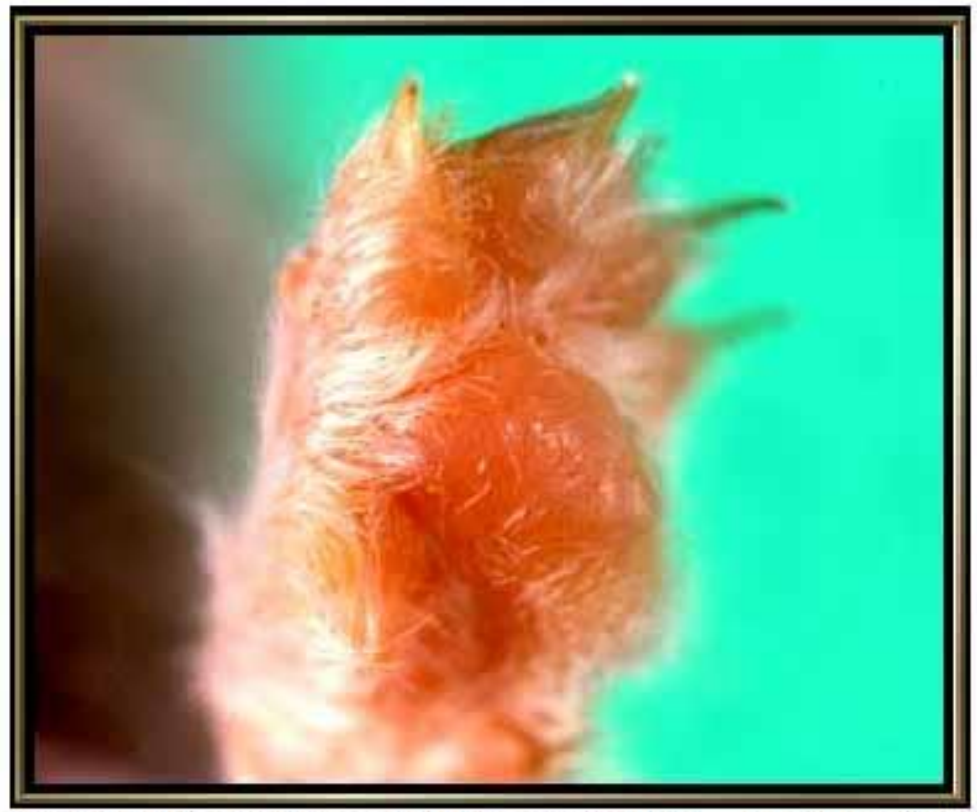
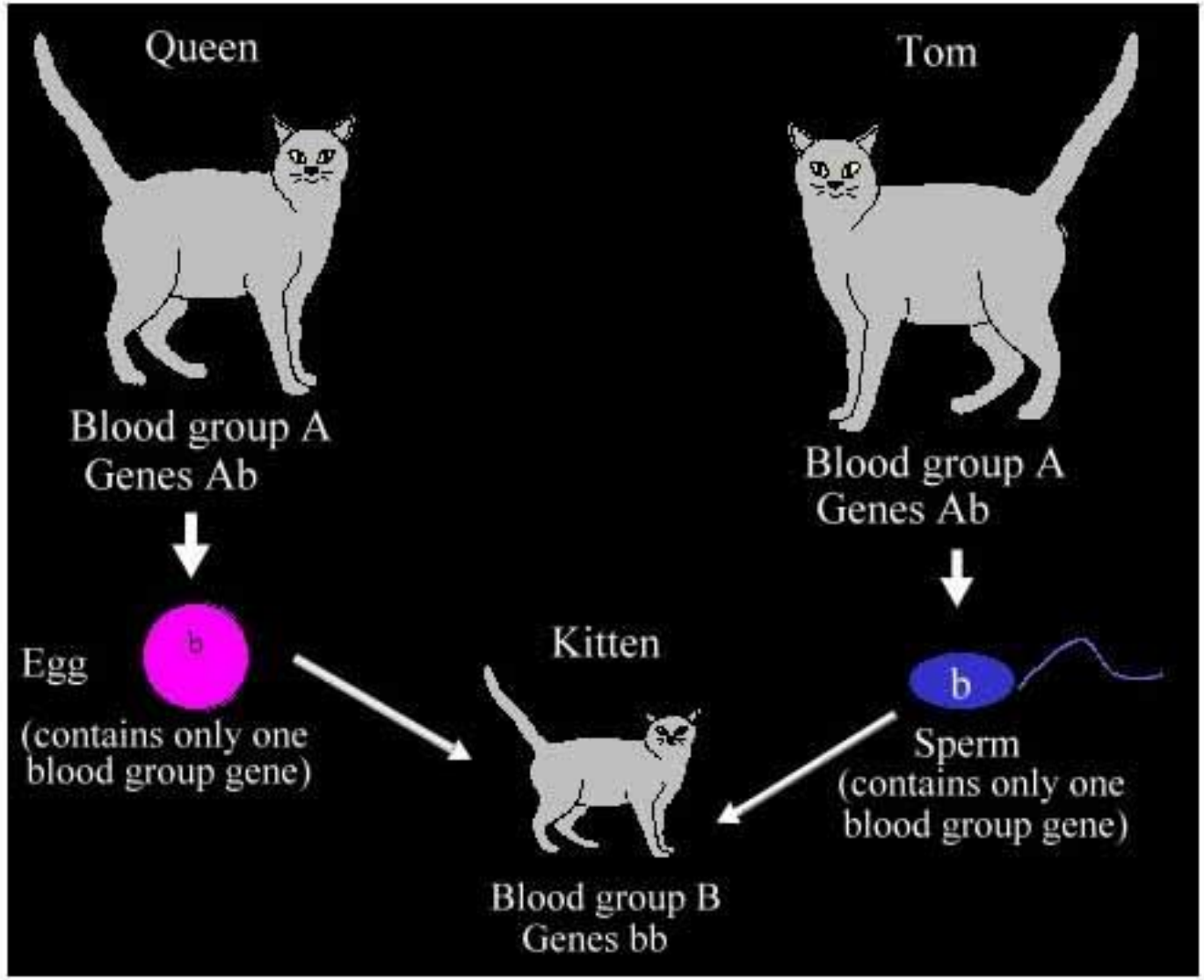


Figure 3.The paw of a kitten with neonatal isoerythrolysis – note how jaundiced (yellow) it looks.


Queen
Tom
Blood group A
Genes Ab
Blood group A
Genes Ab
Egg
b
(contains only one
blood group gene)
Kitten
b
Sperm
(contains only one
blood group gene)
Blood group B
Genes bb

Blood Grouping

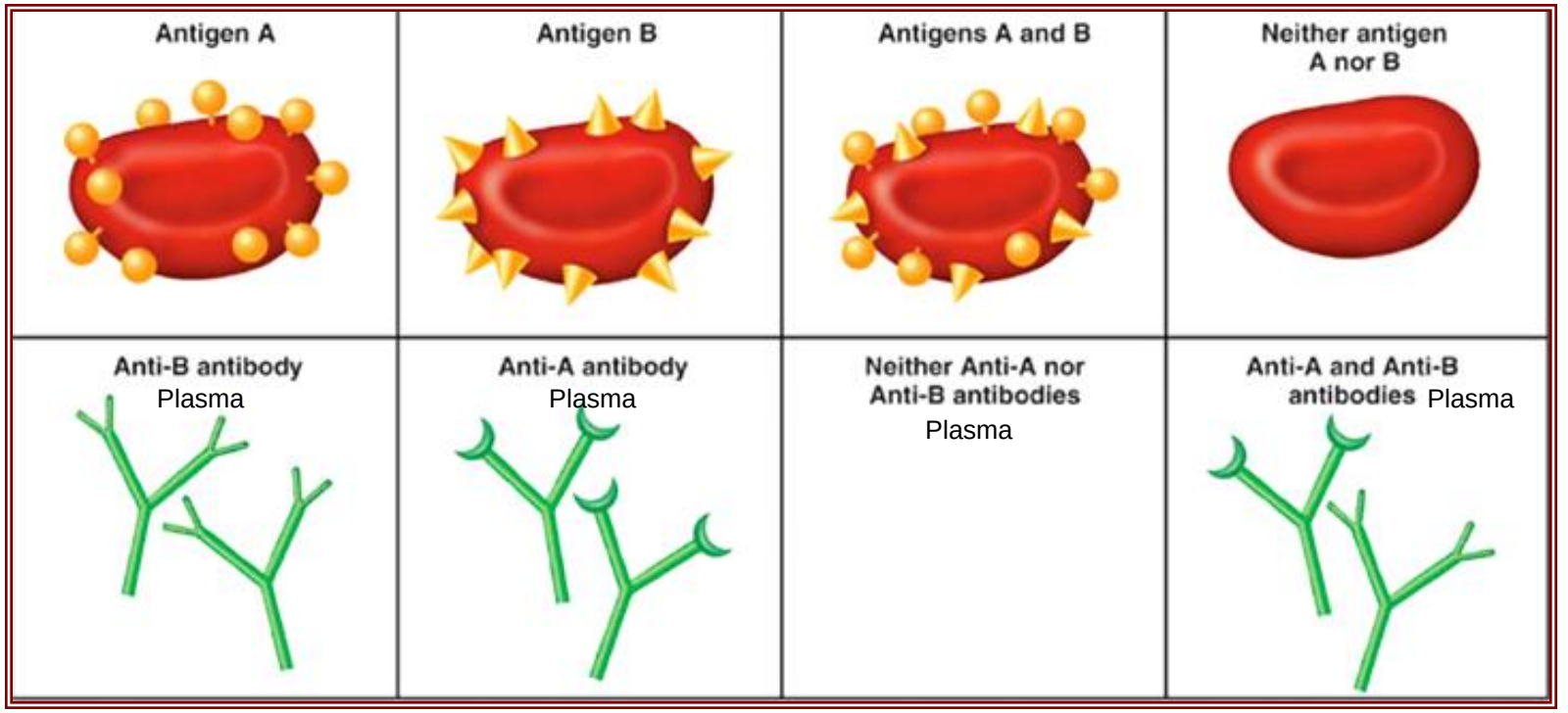
- **Transfusion** is the transfer of blood or blood components from one individual to another.
- **Infusion** is the introduction of fluid other than blood, for example: **saline** solution or **glucose** solution.
- **Blood Group** is determined by the antigens (agglutinogens) on the surface of RBCs.
- **Antibodies** (agglutinins) can bind to RBC antigens, resulting in agglutination (clumping) or hemolysis (rupture) of RBCs
- **Blood Groups**:

ABO Blood Typing

Blood Type	Antigens (Agglutinogens) on Red Blood Cells	Antibodies (Agglutinins) in Plasma
A	**A**	**Anti-B**
B	**B**	**Anti-A**
AB	**A & B**	**None**
O	**Neither**	**Anti-A & Anti-B**

http://learn.genetics.utah.edu/content/begin/traits/blood/

ABO Blood Groups

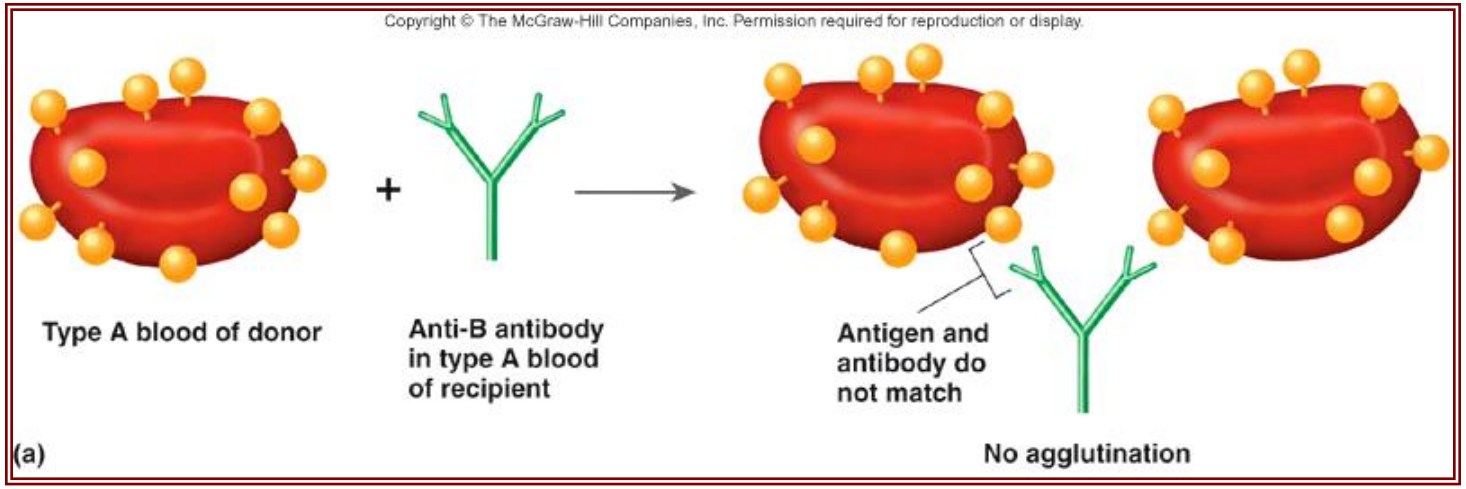


Blood Transfusion

Blood Group	Prevalence	Blood Rec.
O	****	Only O
A	***	O or A
B	**	O or B
AB	*	All

- If the wrong blood type is used, the person's own immune system immediately attacks the donor's blood and causes clots and RBC destruction that can lead to total kidney failure and death.

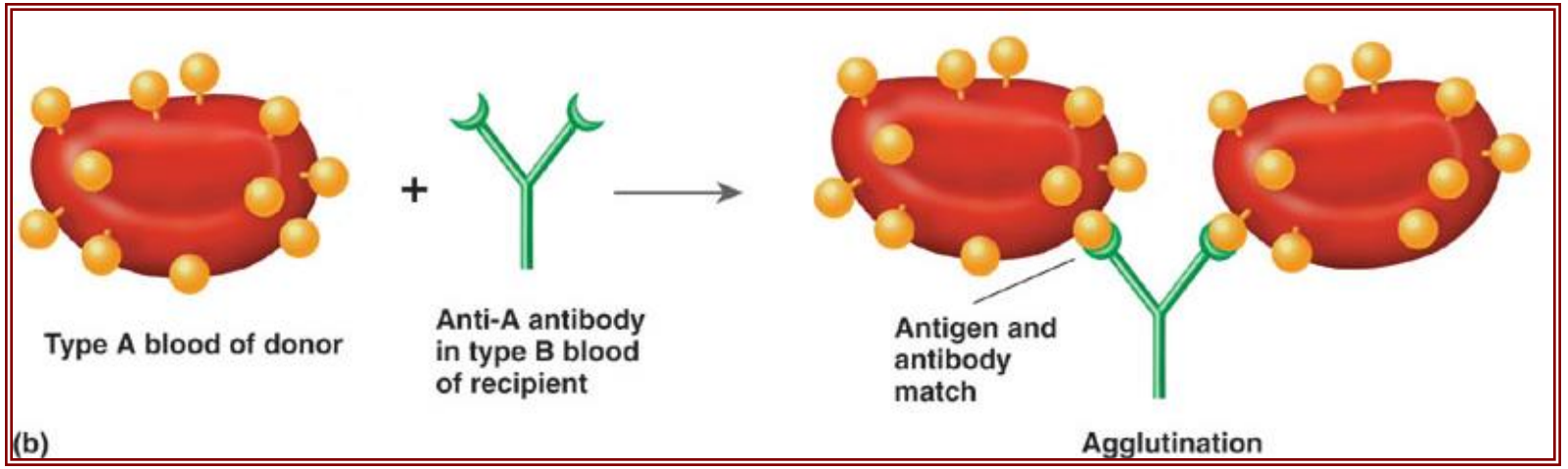
No Agglutination Reaction



- A person with blood type *A* can receive blood from a donor with blood type *A*.
  - The *anti-B* antibodies in the recipient **do not** combine with the type *A* antigens on the red blood cells of the donor.

Agglutination Reaction

- A person with blood type *B* cannot receive blood from a donor with blood type *A*.
  - The *anti-A* antibodies in the recipient will combine with the type *B* antigens on the red blood cells of the donor.



Feline acute transfusion reactions may occur within seconds of a type B cat receiving type A or AB blood. These have an initial phase (lasting for several minutes) that may include restlessness, vocalization, salivation, urination, vomiting, diarrhoea, collapse, mydriasis, hypotension, bradycardia, arrhythmia, apnoea/hypopnoea or seizures. There is then a second phase of tachycardia and tachypnoea, arrhythmia and hypertension with a gradual return to normality in around an hour. Haemoglobinaemia and haemoglobinuria may occur if there is acute intravascular haemolysis.

Delayed reactions may occur 3–21 days after transfusion and relate to haemolysis of transfused cells (usually extravascular, without haemoglobinaemia or haemoglobinuria) with mild pyrexia and anorexia. Mismatched transfused RBCs will have a much shorter survival period (minutes to days, depending upon the titre of alloantibody in the recipient) than the 30–38 days that is standard for matched transfusions.

- Iron overload: cardiac, hepatic and endocrine damage

Fresh frozen plasma

- Plasma frozen within 6 hours of collection
- Contains all the coagulation proteins and inhibitors
- Used if massive transfusion and dilutional coagulopathy, in liver disease and DIC

Platelets

- Correct bleeding due to thrombocytopenia
- Work for lack of production or perippheral consumption
- Not useful if deficiency is due to immune anti-platelet antibody

Intravenous immunoglobulin

- Pooled immunoglobulin
- Used for immunodeficiency, congenital or acquired
- Used in some auto-immune diseases

Clip slide

Early hazards

- ABO incompatibility reaction – can be rapidly fatal
- Fluid overload, pulmonary oedema
- Febrile reactions, urticarial reactions, occasionally life threatening respiratory failure
- Bacterial and malerial infection